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THE SURGICAL TREATMENT OF INTRACTABLE ULCERATIVE COLITIS

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ACUTE DIVERTICULITIS AND SIGMOIDITIS

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LYMPHOGRANULOMA VENEREUM

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DISCUSSIONS BY

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THE SURGICAL TREATMENT OF INTRACTABLE ULCERATIVE COLITIS*

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THE recent revival of interest in the surgical treatment of ulcerative colitis is evidence of the fact that, in a considerable percentage of the cases, conservative or medical therapy leaves much to be desired. There is general concurrence by all authorities that ulcerative colitis is primarily a medical disease and that the great majority of patients will respond sufficiently to conservative therapy to permit them to carry on in relative comfort. However, there remains a group, variously estimated at between 10 and 20 per cent, which resists every form of medical treatment and in whom the pathologic process in the colon progresses to irreparable involvement. It is with this group that this communication is concerned.

The management of ulcerative colitis is a cooperative problem and my associates and I have been most fortunate in having the advice and counsel of Drs. B. B. Crohn and Asher Winkelstein of the Gastro-Enterologic Department, as well as the entire Medical Staff. We have leaned heavily upon them from time to time and wish to acknowledge our indebtedness.

Time does not permit of an extended discussion of the symptomatology, pathologic features, and the many varieties of medical therapy. Suffice it to say that the disease, of unknown origin, is a progressive inflammatory condition of the colon which may be diffusely or segmentally involved. It is characterized by ulceration, infiltration of the colonic wall by the products of inflammation, and the formation of scar tissue. Polypoid degeneration of the mucosa is a not infrequent sequela. There are exacerbations and remissions with gradual progression of the pathologic process until the colon is converted into a greatly thickened, fibrotic, shortened tube, lined by infected granulation tissue constantly exuding pus and blood. The progress of the disease in the colon is reflected in the patient's general condition. Because of frequent rectal discharges with associated loss of fluids, and the general toxemia caused by absorption from the diseased bowel, gradual physical deterioration takes place with weight loss, anemia, avitaminosis and toxic manifestations such as fever, arthritis, skin infections, *etc.* When the colon has reached the stage of such involvement, the disease has become intractable, and it is useless to expect restoration to normal by conservative means.

The surgical treatment of ulcerative colitis, in the past, consisted of ap-

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pendicostomy, cecostomy and, occasionally, colostomy. The purpose of these procedures was to permit of irrigation of the diseased bowel with medicated solutions in the hope of restoring the mucosa to normal. Experience, in recent years, has shown that this therapy was based upon fallacious reasoning. It is important to emphasize that the first requisite of successful surgical treatment is complete diversion of the fecal stream from the diseased bowel segment. This cannot be accomplished by appendicostomy, cecostomy or loop colostomy.

When the treatment of ulcerative colitis as a group problem was undertaken in this hospital in 1937, it soon became evident that it would be necessary to establish criteria for surgical therapy. We are now agreed that surgical treatment is indicated under the following conditions: (1) Uncontrollable hemorrhage. (2) Acute ulcerative colitis with profound toxemia. (3) Impending perforation. (4) Chronic colitis resisting all forms of medical therapy. (5) Segmental ulcerative colitis.

In group one are included cases of repeated large hemorrhages from the bowel, due to erosion of large vessels and resulting in a rapidly developing anemia. The mortality rate in this group, if untreated, is high. Complete diversion of the fecal stream by the performance of ileostomy will put the diseased bowel at rest and minimize the likelihood of further bleeding. We have had three such cases in our series and all recovered. Bleeding may continue for two or three days after ileostomy is performed, but it does not reach the serious proportions noted before operation.

The cases in group two constitute a difficult problem. The course of the disease is short and fulminating and the patients are desperately ill. A fatal outcome is not infrequent. From our experience to date, we are convinced that the *early* performance of ileostomy is a life-saving measure. Unfortunately, heretofore, ileostomy was deferred until the patients were practically moribund. Obviously, the death rate was very high and, as a result, the procedure came into disrepute. It is most important that ileostomy be performed at the opportune moment. In our series, we have had six such cases. One patient died after operation.

Whenever, during the clinical observation of a patient with ulcerative colitis, signs of threatened perforation of a colonic ulcer become evident, ileostomy should be performed as an emergency measure. Only by diminishing intracolonic pressure by diverting the fecal stream, can actual perforation be prevented. When perforation does take place, the mortality rate is close to 100 per cent. In our series, two patients presented symptoms strongly suggestive of imminent perforation and ileostomy was performed as an emergency measure. Both patients survived.

The fourth group comprises the intractable cases of chronic ulcerative colitis. With the aid of the barium enema and careful sigmoidoscopic examination, it is possible to accurately determine the extent and severity of the disease. It is upon these findings and the clinical course of the disease that the decision is made as to the plan of surgical attack. In most instances, a

preliminary ileostomy will be indicated. We have considered ileostomy as the first step of a graded multiple-stage operation involving subtotal resection of the colon. Every patient in our series of 25 cases has been treated according to this plan. However, in the cases presenting complete involvement of the colon and rectum, we have varied the procedure recommended by Cave, Cattell and others, insofar as we are not performing abdominoperineal removal of the rectum, but preserve that organ for possible future use in re-establishing intestinal continuity. The only contraindications to this plan are the presence of rectovaginal fistulae and polypoid degeneration of the rectal mucosa. This will be referred to later.

With the cases of segmental colitis, it may be possible to vary the plan of procedure already described. The type of operation selected will depend upon two factors: (1) The general condition of the patient; and (2) the site of involvement of the colon. When the left colon and rectum are involved, the performance of a transverse colostomy in preference to an ileostomy must be seriously considered. In such cases, complete transection of the colon and its *mesentery* and implantation of the colostomy stomata in separate incisions, after the manner of ileostomy, is obligatory. This is followed at a later date by removal of the diseased left colon. We are treating two patients in this manner. If the rectum is free of disease, an ileoproctostomy with transection of the ileum and also the colon proximal to the site of anastomosis may be the preliminary procedure of choice. Removal of the entire colon may be carried out at a later date. When the right colon alone is involved, the solution of the problem is a simple one. Ileosigmoidostomy with transection of the colon proximal to the anastomosis as advocated by Berg is the operation of choice. It is important to emphasize the fact that the colon must be transected above the site of every anastomosis in order to prevent progression of the disease to the uninvolved segment of bowel. This transection should include the mesentery. It is my impression, after observing the life history of this disease, that progression of the pathologic process takes place along the subserosal and mesenteric lymphatics as well as by the submucosa. Complete division of the bowel and its mesentery should obviate further extension.

Ileostomy.—There are a number of points concerning the operation of ileostomy which merit emphasis. There are so many objections to the old loop ileostomy that I believe this procedure should be discarded. A properly performed ileostomy should entail complete division of the ileum, the implantation of the proximal and distal stomata in separate incisions, and insurance against retraction of either stoma within the abdomen, and also external prolapse of the proximal stoma after it begins to function. About two and one-half years ago, we developed a new type of ileostomy which has satisfied all of these criteria. Recently, Cattell described a similar operation. Figures 1 and 2 indicate the essential steps. The abdomen is opened through a two-inch subumbilical, right rectus incision close to the midline. If the operating table is placed in Trendelenburg position, the loops of small bowel fall away toward the upper abdomen and the terminal ileum may be easily

visualized without handling and manipulation. I cannot emphasize too strongly the necessity of scrupulously avoiding any exploration or manipulation of the diseased colon at this time. In the acute cases, the wall of the bowel is very often of tissue paper thickness and the lightest touch of a sponge stick will result in perforation after a day or two. I am sure that many of the reported deaths after ileostomy may be attributed to ill-advised exploration of the colon.

A loop of terminal ileum is drawn out of the abdomen and its mesentery is divided about eight inches from the ileocecal junction. The vessels in the

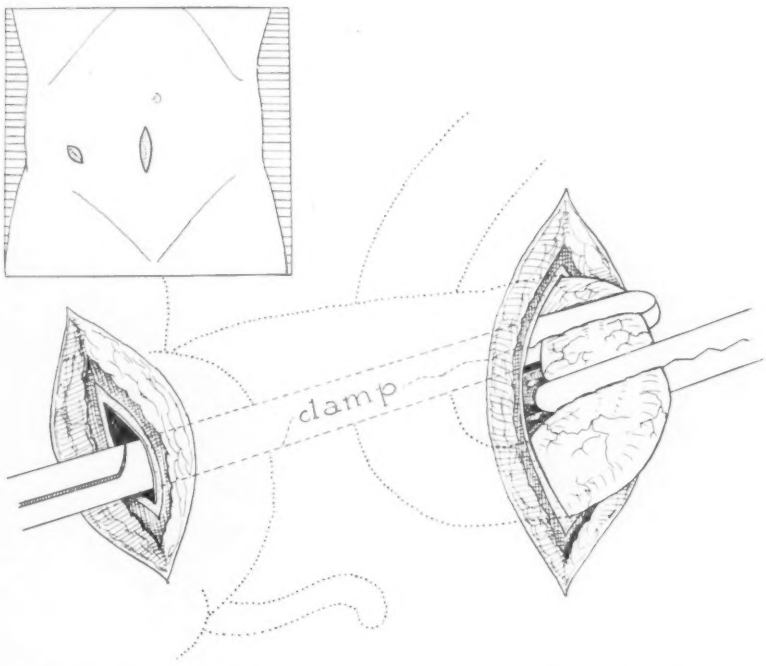

FIG. 1.—Operation for Ileostomy. The right rectus incision should be small and placed close to the midline. The proximal stoma is implanted in this incision, and the distal stoma is placed in the small McBurney incision.

distal two arcades are ligated, care being taken to insure adequate blood supply to the two ileal stomata. Through a one-inch right McBurney incision, a Payr clamp is inserted toward the rectus incision and is placed over the ileum. Another small crushing clamp is now applied to the ileum near the first one in such a way that the antimesenteric portion of bowel faces cephalad. The bowel is now divided between the clamps with the carbolic acid cautery. By proper elevation of the abdominal wall, the clamp protruding through the McBurney incision is withdrawn with the distal ileal loop. The bowel wall is sutured loosely to the fascia with a few fine chromic sutures and the wound is left open. The clamp remains in place until the fourth or fifth day. This forms the distal ileostomy stoma (Fig. 1).

The proximal loop is now drawn out at the upper angle of the rectus incision so as to project beyond the skin surface for three-quarters of an inch. As the peritoneum is repaired, the cut edge of the divided mesentery is included in each suture (Fig. 2). I believe this maneuver anchors the ileostomy in place and prevents the prolapse which was formerly a frequent disagreeable complication of ileostomy. We have not seen a single case of prolapse since we began employing this procedure. The bowel wall is sutured loosely to the neighboring fascia with vaselinized fine chromic catgut. The remainder of the rectus incision is closed in the usual manner. As a final step, a purse string suture of silk is placed in the bowel wall just below the blades of the

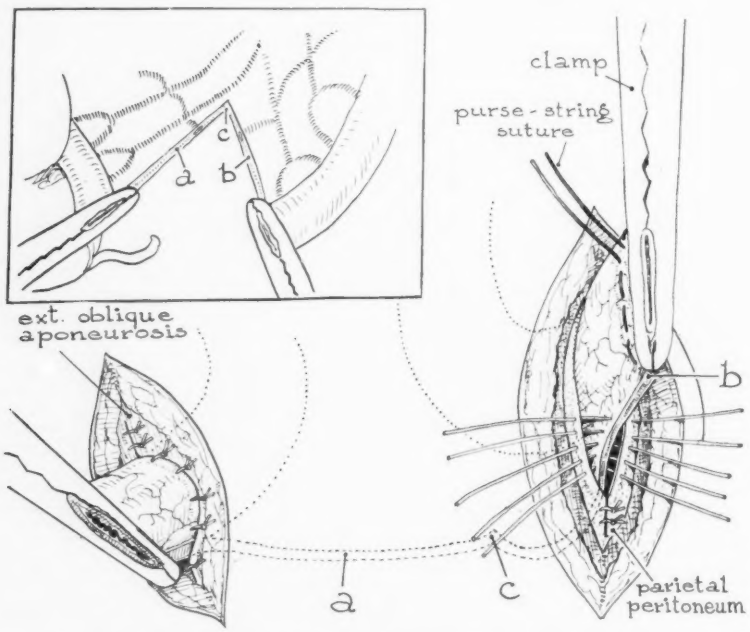

FIG. 2.—The insert shows the division of the mesentery of the terminal ileum. It will be noted that the proximal ileostomy is placed in the wound in such a manner that the antimesenteric border faces cephalad. As the peritoneum is repaired the cut edge of the mesentery is included in each suture. The bowel wall is anchored to the fascia with a few interrupted sutures. The distal stoma is located in the McBurney incision, and the bowel wall is likewise sutured to the fascia. The purse-string suture beneath the clamp occluding the proximal stoma is indicated. This is utilized on the second day, when a large catheter is inserted into the bowel.

crushing clamp. The ends of the suture are tied and wound loosely about the bowel. The crushing clamp is removed in 24 to 36 hours and a large catheter is placed in the bowel and held in place by tying the silk purse string suture. On the fifth or sixth day, the catheter is removed and the ileal stoma is left open. With this technic, we have had only one superficial wound infection.

Our experience with 15 cases of ileostomy has crystallized a number of clinical facts which deserve emphasis:

(1) In the hemorrhage group, severe bleeding usually stops after ileos-

tomy. There may be a moderate hemorrhage or two during the first two or three days postoperative, but these are controlled by transfusions.

(2) In the acute, fulminating cases of colitis and the chronic cases with fever, ileostomy is usually followed by a dramatic change in the condition of the patient. The temperature drops rapidly to normal, often by crisis, and the numerous toxic manifestations abate.

(3) As time goes on, the rectal discharges decrease in amount and rarely contain blood.

(4) There is a gradual gain in weight. Most of the patients have gained between 20 and 40 pounds. This is accompanied by a sense of well-being which does much to raise the morale of these patients.

(5) We have not encountered a single instance of reactivation of the process in the colon or a return of acute toxic manifestations, once the colon has been excluded by ileostomy.

(6) The discharge from the ileostomy stoma is liquid in the beginning. In the course of a few months, coincident with gain in weight and improvement in the patient's general condition, the ileal contents gradually become semisolid. This change in the physical characteristics of the contents of the terminal ileum becomes even more pronounced after removal of the diseased colon. It would seem that a change takes place in the physiologic activity of the small bowel and that the ileum takes over the water-absorbing function of the diseased colon.

(7) There is always a certain amount of skin irritation surrounding the ileostomy stoma. It is usually more pronounced in the beginning. A considerable degree of local tissue resistance is developed as time goes on and, rarely, does this irritation bother the patient after three or four months. Most of the patients use a mixture of kaolin and aluminum paste to protect the skin. The discharges from the ileum are taken care of without soiling by a properly-fitting ileostomy bag.

(8) It is wise to defer resection of the colon until the maximum improvement has been obtained, usually six to 12 months.

(9) It is our opinion that ileostomy should, in no sense, be considered a curative operation. We have observed active disease still present in the colon 18 months after its exclusion by ileostomy. Reestablishment of continuity of the ileum is fraught with great danger. The literature contains a number of such instances in which a fatal issue followed the lighting up of a dormant process in the colon.

Further Operative Procedures.—Subtotal resection of the diseased colon should be carried out after the limit of improvement has been reached. If proctoscopic and sigmoidoscopic examination indicates a normal rectum and lower sigmoid, the first stage should consist of an anastomosis between the ileum and the anterior wall of the rectum. In the five patients, in whom ileoproctostomy was performed, the disease in the colon was found to terminate sharply just above the rectosigmoid junction. In each instance, the bowel was divided at this point, the distal end was inverted, the proximal

end was implanted in the upper angle of the left rectus wound to form a colostomy opening, and an isoperistaltic lateral anastomosis effected between the ileum, after disconnection of the ileostomy, and the anterior wall of the rectum. All healed by primary union without evidence of leakage. It should be emphasized that, when dealing with the bowel of an ulcerative colitis case, no blind ends be dropped into the abdomen, and that instead of inverting the end of the divided colon to be subsequently removed, the bowel end should be implanted in one angle of the incision as a colostomy opening. This will permit external drainage of discharges from the diseased segment. This important point has already been stressed by Berg. The next stage, carried out after two or three months, consists of removal of the sigmoid, descending, splenic flexure and left half of the transverse colon. The remaining colon end is again implanted in the wound. All raw surfaces are peritonized and the left retrocolic space is drained. The final stage consists of removal of the terminal ileal fistula and the remainder of the colon.

When the disease has involved the rectum as well as the remainder of the colon, our plan of attack has consisted of subtotal resection of the colon in two stages, starting on the left side, and leaving the lower sigmoid and rectum *in situ* for possible future use in reestablishing intestinal continuity. Whether the latter will be possible, time alone will tell. So far we have not carried it out. It has been our feeling that, unless the rectum is hopelessly diseased by pseudopolypoid degeneration or the presence of numerous fistulae, time, measured in terms of years, might eventually heal the lesion in the rectum and permit restoration of normal elimination. Our cases have not been followed long enough to warrant making definite statements relative to this, but in three instances, there has been marked improvement in the proctoscopic picture. Whether the rectal segment will be converted into a scarred tube, unsuitable for anastomotic purposes or develop strictures, we are unable to say. Continued observation will be of great interest.

At this stage, the upper half of the sigmoid, the descending colon and the left half of the transverse colon are mobilized and brought outside of the abdomen. The left retrocolic space is peritonized and the left rectus wound is closed about the two limbs of colon, the proximal limb being located at the upper angle of the incision and the distal limb at the lower angle. Only after the incision has been sutured, is the bowel divided between rubber-covered clamps and removed. This maneuver minimizes the possibility of wound contamination. The final stage, performed three to six months later, consists of excision of the remainder of the colon and the distal segment of ileum. In order to remove the field of operation from the ileostomy opening, we have used the upper abdominal transverse incision, cutting across both rectus muscles. If the patient is placed in Trendelenburg position, mobilization of the distal ileum and ascending colon is made easier. Before opening the abdomen, it is preferable to dissect the colostomy and ileostomy stomata from their respective scars and invert the bowel ends so as to avoid contamination. The right retrocolic area is drained through the right McBurney incision,

which marked the site of the distal ileostomy opening, and the transverse incision is closed snugly.

The patient now has two openings on the abdominal wall, one marking the ileostomy and the other, the colostomy leading into the distal sigmoid. The purulent discharge from the rectal segment gradually decreases in quantity and the patients show progressive improvement. Up to the present, we have not seen the need of excising the rectum in any of our cases. Whether this will prove to be the correct procedure, we are not prepared to say at this time. Prolonged observation of these patients will be necessary before this can be decided.

Results.—Our series consists of 25 patients treated surgically since September, 1937. In 15 cases, ileostomy was performed, with two deaths, a mortality rate in this group of 13.3 per cent. The first death occurred in the case of a male, age 21, with a one year's history of bloody diarrhea and recent onset of toxic symptoms with repeated hemorrhages. At operation, a sponge stick inadvertently touched the cecum. The patient died on the sixth day and, at autopsy, there were found two perforations of the cecum and one in the transverse colon with a diffuse peritonitis. The second patient, a female, age 18, presented symptoms of three months' duration. After ileostomy, there was satisfactory progress until the sixth day. She then began to deteriorate rapidly, presenting the picture of secondary anemia, hypoproteinemia, and peripheral edema. In spite of multiple transfusions, parenteral administration of vitamins and supportive therapy, death ensued on the eleventh day. At autopsy, there was found a necrotizing esophagitis and complete atelectasis of the left and of most of the right lung.

Of the remaining 13 cases, resection has been completed in eight patients according to the plan outlined in this paper. In two of these, ileoproctostomy was performed prior to removal of the diseased colon. There was one death in the resection group. This patient died of an avoidable accident, as at the final stage, it was found difficult to close the left end of the upper transverse incision and, accordingly, packing was inserted to wall-off the peritoneum. Premature removal of the packing permitted gross soiling of the peritoneal cavity by ileostomy contents and the patient died of diffuse peritonitis. This was demonstrated at autopsy. In four cases, resection of the left colon has been carried out and the patients are awaiting the final stage. The remaining patient has not as yet been subjected to further surgery since ileostomy was performed. All of these patients are doing well. There is minimal discharge from the remaining rectal segment and all have gained 20 to 30 pounds. The two patients with ileoproctostomy have one to three normal bowel movements a day and proctoscopic examination reveals normal rectal mucosa.

In the group of segmental ulcerative colitis, there were eight cases. In two of these, the disease involved the left colon and rectum, and transverse colostomy was performed with implantation of the proximal and distal stomata in separate incisions. Both patients have done well. There has been no evi-

dence of extension of the disease to the right colon. Resection of the diseased segment will be carried out shortly. Of the remaining six cases, three were subjected to primary ileoproctostomy followed by removal of the remainder of the colon in one or two stages. One patient recently developed a mild involvement of the rectal segment with hyperemia of the rectal mucosa demonstrable on proctoscopic examination. There has been a rapid response to medical therapy. The other two patients are in excellent health. In the remaining three cases, ileosigmoidostomy was performed as the first stage. In one patient, resection of the colon was completed, and she is well. In the second case, further surgery has not as yet been carried out. The third patient died after operation as a result of an error in judgment. This occurred in a male, age 36, who presented a rather acute history of five weeks' duration. The rectum and sigmoid were uninvolved, and ileosigmoidostomy was performed with division of the colon and its mesentery proximal to the anastomosis. The error was made of exploring the entire colon with the necessarily associated handling of the diseased bowel. The patient died two days after operation and, at autopsy, there was found a generalized peritonitis due to a perforation of the cecum. I believe that this perforation was traumatic in origin and occurred at the time of operation.

The final two cases of the series are classified as miscellaneous. One was a female, age 23, who presented a history of four years' duration. The clinical picture of diarrhea, loss of weight, rectovaginal fistula, moderate pyrexia, anemia and the roentgenographic evidence of involvement of the terminal ileum and ascending colon, suggested to the gastro-enterologists a diagnosis of ileitis with secondary colitis. Ileocolic resection was advised. At operation, the transverse and left colon appeared free of disease externally except for some thickening of the wall. Resection of the right colon was accordingly carried out. When anastomosis between ileum and transverse colon was attempted, extreme friability of the remaining bowel was demonstrated. Gross soiling occurred and the operation was terminated by establishing a double-barreled fistula composed of ileum and sigmoid. The patient died of peritonitis three days later. The operation was ill-advised and based upon an erroneous diagnosis. The second patient presented a long and complicated history. Briefly, her disease started in the terminal ileum in 1929, and the ileum was resected. A diffuse ulcerative colitis developed subsequently. The second operation consisted of an ileosigmoidostomy performed, apparently, in diseased colon. Then followed resection of the colon in two stages. When admitted to the service in December, 1938, she presented numerous abdominal fistulae and rather extensive ulceration of the rectum on proctoscopic examination. Operation was carried out and consisted of (1) resection of the ileosigmoidostomy anastomosis; (2) ileostomy; and (3) implantation of the upper rectal stoma in the abdominal wall. Since then, this patient has done very well. All the abdominal fistulae have closed and the rectal discharge has practically stopped. She has gained 35 pounds.

SUMMARY AND CONCLUSIONS

There were five deaths in this series of 25 patients, a gross mortality of 20 per cent. Analysis of the cases that died indicates that, in four instances, an error of technic or judgment was responsible for the mortality. It is fair to assume, with increasing experience in the surgical treatment of this disease, such errors will become less frequent, and that the mortality will reach well below 20 per cent. I believe that the surgical treatment of intractable ulcerative colitis will, eventually, be generally recognized as the only method at our disposal to-day of restoring these seriously handicapped patients to a relatively normal existence.

DISCUSSION.—DR. HENRY W. CAVE (New York) prefaced his remarks by paying tribute to the courage and the wisdom of Dr. Howard Lilienthal who, assisted by Dr. George Emerson Brewer, 40 years ago, in 1899, performed a colectomy upon a young woman, age 25, who was suffering from this disease in an aggravated form—she survived the operation, lived a normal life, gave birth to a child and died one and one-half years ago, at the age of 63, from a cardiac disease. An autopsy was performed and nothing unusual was to be noted in the abdomen except the absence of the entire colon, and a small rectosigmoidal pouch to which the ileum had been attached, which showed no evidence of disease.

Too long have surgeons followed blindly the idea that all people suffering from ulcerative colitis should be treated medically. It was hoped that Bargen's ideas on the specificity of a certain organism would result in the production of a vaccine which would be curative in most cases. But his contentions have not been substantiated by other investigators. Doctor Garlock states that there is a 10 to 20 per cent group that do not respond medically and should be treated surgically. Doctor Cave felt that as time goes on this group will be found to be much larger than is at present admitted.

Doctor Garlock also states that from time to time he has leaned heavily upon his medical associates; Doctor Cave suggested that he lean even more heavily and more constantly upon them for advice and counsel. This disease is commonly complicated by profound physiologic disturbances, changes in the plasma protein and electrolyte concentrations, inanition and marasmic states, advanced grades of vitamin deficiencies, disturbance of fluid balance and severe, refractory anemias, and is, therefore, better understood by the physician than by the surgeon.

The positive indications for immediate surgery are perforations, impending or actual; repeated massive hemorrhage; the frequently occurring and recurring perirectal abscesses; and those cases that are acutely ill and are apparently overwhelmed by a profound toxemia.

Diversion of the fecal current by transverse ileostomy is essential in a great majority of these patients. In a small group of less than 10 per cent low ileosigmoidostomy can be carried out as the first stage of the procedure. Ileostomy is accompanied by a high mortality rate due principally to the fact that surgical aid is solicited too late, and in many instances fatalities have occurred due to a rapid loss of fluids and chlorides. Doctor Cave cited three instances, in his experience, of alarming bleeding from the colon after ileostomy which was satisfactorily controlled by massive doses of vitamin K. In performing ileostomy the mucous fistula should be placed to the left of the midline so that at the second procedure, which is the more

difficult, due to the remoteness of the splenophrenic colic ligament, it is more easily divided through a long left paramedian incision. Instead of waiting 24 to 36 hours to remove the clamp and insert a large catheter in the ileal stoma, these patients had better have the ileostomy opened immediately following operation. Ileostomy should in no sense be considered a curative operation, but it is rather interesting in talking with various surgeons to hear them report definite cures following this procedure. Doctor William F. Nickel, Jr., of the New York Hospital, recently told Doctor Cave that he had collected seven authentic case reports where patients have remained well from nine to 17 years after ileostomy. In Doctor Cave's opinion cases in which ileostomy has proved to be curative are cases wherein a stage of intractability has not been reached.

With regard to patients with the chronic form of the disease with remissions, unanimity of opinion regarding surgical intervention is difficult to attain. In Doctor Cave's judgment, the patient should be given the benefit of a surgical procedure when the colon becomes transformed into a narrowed, shortened, fibrotic organ lined with infected granulation tissue; and the sooner this conclusion is arrived at the more hopeful is the ultimate outcome for that particular patient.

Doctor Cave disagreed with Doctor Garlock's statement that "in those cases presenting complete involvement of the colon and rectum" he does not perform "abdominoperineal removal of the rectum, but preserves that organ for possible future use in reestablishing intestinal continuity." This is predicated upon the concept that the diseased rectum which is shrunken, fibrotic and infected throughout its coats will return to a degree of normalcy that will safely permit of an anastomosis between it and the healthy ileum. It is hard to believe that this can come about and, if it cannot, it is a violation of a surgical principle to anastomose a healthy loop to another loop that still remains partially diseased. It is generally recognized that in 90 per cent of these cases the rectum is involved. In Doctor Cave's series there has probably been a higher percentage of involvement than in Doctor Garlock's. Cattell cites an incidence where this was attempted and the disease process spread from the rectum quite rapidly up the newly attached ileum and resulted in a fatality. Heuer has told Doctor Cave that he has already performed this operation on two individuals; both are improved but not well, one has developed perineal fistulae and Doctor Heuer plans to take down the anastomosis and remove the diseased rectum. Five of Doctor Garlock's patients were particularly fortunate in having had the disease process terminate so sharply just above the rectosigmoidal junction. With regard to Doctor Garlock's statement that he had not as yet carried out his plan to reestablish the fecal current from the ileum to the rectum that was involved, Doctor Cave felt that Doctor Garlock is perhaps too hopeful that the rectum will rehabilitate itself so that this proposed anastomosis would result in complete cure.

Doctor Cave agreed most heartily that no blind ends should be dropped back into the abdomen and that Doctor Garlock's method of mobilizing and bringing outside the descending colon and not removing it until his incision has been sutured is well worthy of comment and enthusiastic approval, for this maneuver certainly minimizes the possibility of infection. Although Doctor Cave has never employed the upper abdominal transverse incision, he felt that Doctor Garlock's intention of keeping away from the ileostomy opening by so doing is a good one. Doctor Cave said that, although up to the present Doctor Garlock has not seen the necessity of excising the rectum in any of his cases, with more experience he would probably find it necessary. On

account of perirectal abscesses, fistula-in-ano and an active process in the rectum Doctor Cave has had to remove the rectum in six individuals in his series.

In conclusion, Doctor Cave said that the mortality rate in his own series has been higher than that of Doctor Garlock's, there having been seven deaths in 31 patients operated upon, a mortality rate of 22.5 per cent.

DR. JOHN F. ERDMANN (New York) reported the following case of colectomy: The patient, H. S. M., aged 16, was admitted to the New York Post-Graduate Hospital on Doctor Gant's service, with a diagnosis of mucous colitis. An appendicostomy was performed by Doctor Gant. The patient was discharged November 22, 1915. A few weeks later, December 27, 1915, he was readmitted to Doctor Erdmann's service and an ileostomy was performed after the method of John Young Brown. He was again admitted March 27, 1916, with a diagnosis of chronic ulcerative colitis. Colectomy with ileosigmoidostomy was performed. The colon was resected, for ulcerative colitis, down to the midportion of the sigmoid and a lateral ileosigmoidostomy was effected June 3, 1916. The pathologist's report was "section from wall of intestine shows marked increase of adenoid tissue of mucous membrane with loss of the surface epithelium and relative decrease in the number of glands. There is considerable thickening of the submucosa due to increase of fibrous tissue and edema, and in it are some plasma and round cells."

During the patient's tour in the hospital, the hemoglobin varied from 65 to 40 per cent, with a low red count of 3,656,000. He was discharged July 6, 1916. On September 18, 1916, he was readmitted to the hospital for a discharge of blood, which frightened him. After various tests he was discharged September 21, 1916. His blood counts during 1916 were as follows: January 6: 4,160,000, Hb. 40 per cent; March 28: 3,064,000, Hb. 40 per cent; April 10: 4,600,000, Hb. 65 per cent; September 8: 4,848,000, Hb. 82 per cent.

The patient has been examined within the past four years. During the years between there had been no advance in the condition but rather a curative process. He presented all the appearances of a healthy, husky, strong man. It might be said that the patient had a few ulcerated spots in the rectosigmoidal zone, from which would be discharged a very small amount of blood at times.

DR. HENRY F. GRAHAM (Brooklyn) asked what "intractable" really means. In Mt. Sinai and Roosevelt hospitals, for instance, where special thought is given to these cases, it means one thing and elsewhere another. To illustrate the point Doctor Graham cited the case of a woman, at present in the Methodist Episcopal Hospital. She was transferred from another hospital where she was said to have had "intractable" ulcerative colitis for four and one-half years. She is anemic, but her nutrition was very good. When asked if her teeth had been examined roentgenologically, she said, "No." This was done and revealed two bad apical abscesses. Doctor Graham said he did not know, of course, that this patient's condition would be cured by removal of those teeth, but that he had seen patients with severe proctitis improve within two weeks after the removal of abscessed teeth, without an active recurrence. Poor medical treatment may make such cases "intractable."

Doctor Graham then cited a case to illustrate: First, the importance of early ileostomy; second, the importance of including the mesentery in the peritoneal suture to prevent prolapse; and third, the matter of the time interval between operations and the question of removal of the rectum. The patient was a boy, age 22, who developed a streptococcus sore throat in

April, 1937. Two or three months later he had a severe attack of diarrhea, during which he passed 30 to 40 bloody mucous stools daily. He lost 17 pounds during the first month of this illness. After one month in a hospital in New Jersey, he was admitted to the Methodist Episcopal Hospital in October, 1937. During the ensuing 19 days he lost an additional 10 pounds, which reduced his weight to 95 pounds. On November 7, 1937, an ileostomy was performed. Obstruction occurred from edema of the stoma and later a prolapse developed through the stoma. His weight increased to 144 pounds. On February 2, 1938, the cecum and colon were removed down to the sigmoid, for persistence of the colitis. The mesentery of the ileum was sutured to the peritoneum to prevent prolapse. His sigmoiditis and proctitis persisted, and 14 months later (April 19, 1939) the sigmoid and rectum were removed. The wound is now almost healed. Healing has been delayed because of long hours the patient spends driving a truck each day. He now weighs 155 pounds.

Dr. John H. Garlock (closing) said that he had not meant to imply that his medical confreres were consulted only occasionally with respect to the treatment of patients with ulcerative colitis. There has been constant cooperation and collaboration during every phase of this work, and, in most instances, the decision to operate has been made by the gastro-enterologist. The problem of conservation of the rectum is a very important one, but Doctor Garlock felt that most surgeons' experience is not large enough yet, nor has extended over a sufficiently long time, to warrant the statement that every case of diffuse ulcerative colitis requires an abdominoperineal resection of the rectum as part of the multiple-stage operative procedure. If the rectum is hopelessly involved in scar tissue, or presents extensive polypoid degeneration, then resection is indicated. On the other hand, in those cases presenting hyperemia and bleeding of the rectal mucosa on proctoscopic examination, it is not at all established that they should be subjected to removal of the rectum. The actual cause of the disease is unknown, and so is what the future holds with reference to determining that cause. Therefore, Doctor Garlock preserves the rectum in the hope of eventually utilizing it in a certain percentage of cases, to reestablish intestinal continuity. Only time, and a very large experience, will eventually decide this point.

ACUTE DIVERTICULITIS AND SIGMOIDITIS*

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THIS COMMUNICATION is based on 82 personally observed cases, in all of which the symptoms were sufficiently severe to warrant a surgical consultation. All patients were seen as primary cases, during the acute stage, except three, which had had a resection performed at another institution, and came to us with a colostomy. In one of these an acute attack of diverticulitis had developed in the segment of sigmoid remaining after resection of the originally involved portion, and required drainage. A second case was admitted with thoracic empyema and pyonephrosis, 18 years after a sigmoid resection. She is included simply as a late-result. The third case desired closure of her colostomy.

Many of the patients had a history of previous intestinal symptoms similar to those for which they were seen by us. The majority recovered under conservative management. Some were admitted as surgical emergencies and had to be operated upon at once. Others were operated upon for the relief of symptoms or to rule out malignancy. All patients have been kept under observation. Many have had no subsequent serious symptoms, while others have been seen several times with recurrent attacks.

The majority belonged to the somewhat better situated class as indicated by the fact that 65 were private cases and only 17 were ward cases. No conclusions, however, can be drawn from this, because there was nothing exceptional in their mode of living or habits which seemed to have a bearing on the etiology, except perhaps constipation. Adiposity does not seem to be a factor.

Our reason for presenting these cases is to call attention to the frequency of the condition and especially to the serious complications which may be associated with it and which require prompt surgical attention.

Age and Sex Distribution.—The disease was most frequently encountered in the age-group between 50 and 60 years. Thirty-one, or 37.9 per cent, occurred during this period. The others are distributed as indicated in Table I. There were 41 women and 41 men in the group.

TABLE I

AGE DISTRIBUTION OF 82 CASES

	30–40	40–50	50–60	60–70	70–80	80–90
Number of Cases.....	6	13	31	20	10	2

Symptoms and Physical Signs.—In order of frequency, the following symptoms and physical signs were noted (Table II):

* Read before the New York Surgical Society, New York, N. Y., October 25, 1939. Submitted for publication October 7, 1939.

TABLE II

FREQUENCY OF OCCURRENCE OF SYMPTOMS AND PHYSICAL SIGNS

Symptoms	Number of Cases	Per Cent	Symptoms	Number of Cases	Per Cent
(1) Pain	82	100.0	(8) Gas	21	25.6
(2) Fever	56	68.3	(9) Perforation	20	24.4
(3) Constipation	56	68.3	(10) Vomiting	19	23.2
(4) Palpable tumor	37	45.2	(11) Urinary symptoms	16	19.5
(5) Leukocytosis	34	41.5	(12) Bleeding	16	19.5
(6) Cramps	28	34.2	(13) Loss of weight	15	18.3
(7) Obstruction	24	29.3	(14) Diarrhea	15	18.3
			(15) Associated carcinoma	5	6.1

Diagnosis.—(A) Uncomplicated Cases: The most important point in reaching a diagnosis is to bear the condition in mind when patients with suggestive symptoms present themselves. Lower abdominal pain, with cramps, gas, fever, and perhaps alternating constipation and diarrhea, should cause one to think of a sigmoid lesion. Tuberculosis, syphilis, polypi, simple ulcerations or endometrial implants have to be considered. Pelvic disease, which may simulate the symptoms of diverticulitis, should not present a serious diagnostic problem. The two important lesions which come under consideration are carcinoma and diverticulitis. In order to make a correct differential diagnosis, it is necessary to properly evaluate symptoms, to utilize all physical signs and to have good roentgenologic examinations. It is usually not one symptom or sign but a combination of several which makes a positive diagnosis possible.

A prolonged history of disability, with progressive symptoms of constipation, cramps, blood in the stool, a palpable tumor and perhaps loss of weight, favor the diagnosis of carcinoma. On the other hand, if the symptoms are of short duration, if pain is an outstanding symptom, and if there is fever and leukocytosis, a history of former attacks, and examination shows tenderness and rigidity, the diagnosis of diverticulitis is more likely.

Neither condition is an emergency, and one may follow conservatism until a definite diagnosis is possible. The age of the patient is of no diagnostic value because both conditions affect the same age-groups. The course of the disease, on the other hand, may aid a great deal. With bed rest, fluid diet, hot or cold applications, and careful low rectal irrigations, the acute signs may quickly disappear, and permit careful physical examination.

There are, of course, patients in whom the symptoms are much more severe. They may be acutely ill with pain, fever and obstructive symptoms. There may be doubt whether local perforation has taken place. At times, urinary symptoms predominate. Good judgment is required in directing treatment. All colonic instillations must be avoided until acute symptoms and signs have subsided.

Digital rectal examination can do no harm. Proctoscopic examination, on the other hand, is not indicated. The greatest aid in the differential diagnosis

is a roentgenologic examination after the administration of a barium clysma. It is important not to use force for fear of causing a perforation. The following procedure should be followed: (1) Flat film. (2) Fluoroscopy—watching the barium mixture flow in, with only slight manipulation. (3) Take roentgenograms in different positions, including oblique and lateral. (4) Take subsequent roentgenograms after six and 24 hours. (5) If sufficient information is not obtained, careful air inflation may be of value.

Stewart[1] has compiled a tabulation on the differential diagnosis between

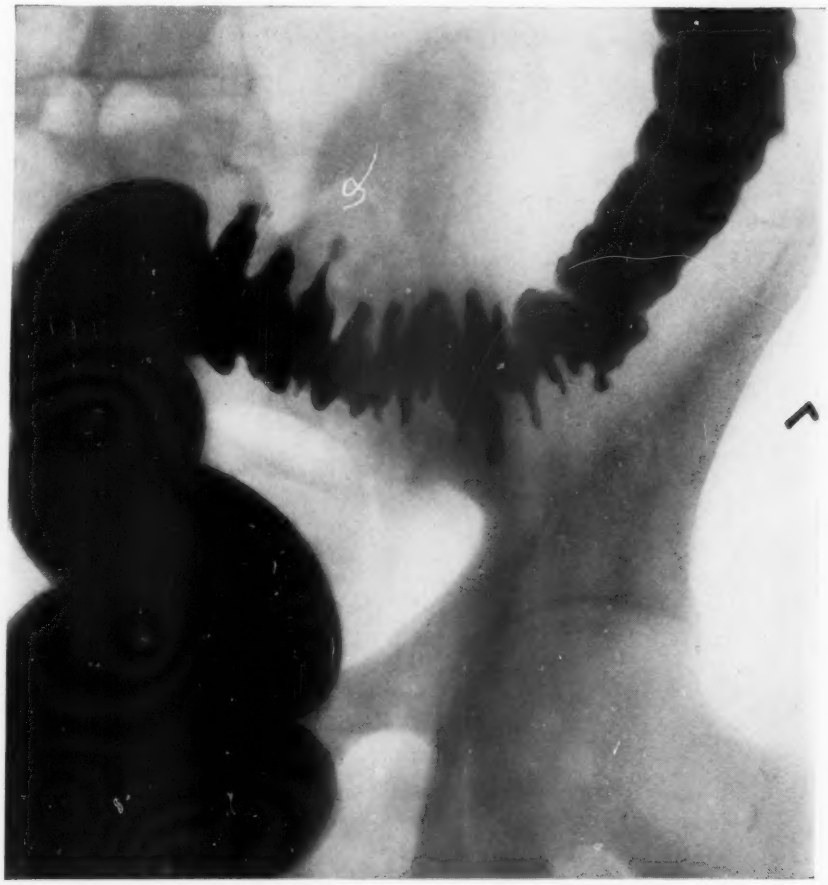

FIG. 1.—Typical serrated appearance of acute sigmoiditis.

carcinoma and diverticulitis which is very helpful. Not all the differential points mentioned by him can be elicited in any one case. The important and common differences between the two conditions are as follows: In diverticulitis, there is involvement of a long segment with its lumen narrowed and presenting a serrated appearance. It shows spasm, perhaps one or several diverticula close to the lesion, and is tender to touch (Fig. 1). In carcinoma the haustral markings are destroyed and there is either a napkin-ring or mas-

sive deformity with crater formation (Fig. 2). Notwithstanding such careful study, however, a positive diagnosis cannot be made in some cases, and serious doubt remains. In some patients a short period of observation will aid, while in others an exploratory celiotomy is indicated. Even then, it is not always

FIG. 2.—Carcinoma of sigmoid associated with acute sigmoiditis.

possible to make a positive diagnosis and resection has to be resorted to (Figs. 3 and 5).

The relative frequency of the two conditions may be judged on the basis of gastro-intestinal roentgenologic studies, made at our hospital, during the course of one year (Table III):

TABLE III

INCIDENCE OF DIVERTICULITIS, DIVERTICULOSIS, AND CARCINOMA

(*Lenox Hill Hospital, November* 1, 1938–*October* 31, 1939)

Gastro-intestinal series (total)	902	
Terminated at 6 hrs.	255	
Carried through 24-hr. period	647	
Diverticulosis diagnosed in	49	or 7.5%
Barium enemata	428	
Diverticulosis diagnosed in	58	or 13.5%
Diverticulitis associated with diverticulosis	18	or 31.0%
Carcinoma of sigmoid	31	or 7.2%

(*B*) *Complicated Cases with Perforation.*—The clinical picture is quite different when diverticulitis is complicated by perforation. When first seen,

FIG. 3.—Acute sigmoiditis. Resected because suspicious of carcinoma. (Also see Fig. 5.) Same patient.

the patient may have a spreading peritonitis, the origin of which is doubtful. The onset, with acute pain on the left side, and a history of previous attacks of pain on that side, may help one. In case there is an abscess, it is most likely on the left side and, therefore, easy of diagnosis. When situated in the pelvis or lower midabdomen, a positive diagnosis may not be possible until after opening the abdomen. If the abscess is small, localized in the mesentery, or plastered against the sigmoid or the pelvic wall, the symptoms

and signs are relatively mild and permit study and observation. A late diagnosis may be reached the same as in uncomplicated cases (Fig. 4). In all other patients, we are dealing with acute surgical emergencies requiring prompt attention. The indication is to operate and to make a diagnosis after

FIG. 4.—Ruptured diverticulum of sigmoid which could be lifted out with the inflammatory mass. Resection was performed.

incision; and then to handle the problem presenting itself according to one's best judgment.

(*C*) *Diverticulitis Resulting in Intestinal Obstruction.*—When a patient is seen with symptoms of intestinal obstruction, the differential diagnosis between diverticulitis and carcinoma is very difficult and may be impossible (Figs. 2, 3 and 5).

The pain associated with acute diverticulitis is usually more severe, apparently due to muscle spasm of the intestine. The patient may be covered with perspiration and appear shocked. The presence of temperature and leukocytosis may be of aid. There may be a history of former attacks.

In obstruction due to carcinoma of the sigmoid, there is usually a history of continuous and slowly increasing disability. A tumor may be palpable, without much tenderness or rigidity. Blood may have been noticed in the

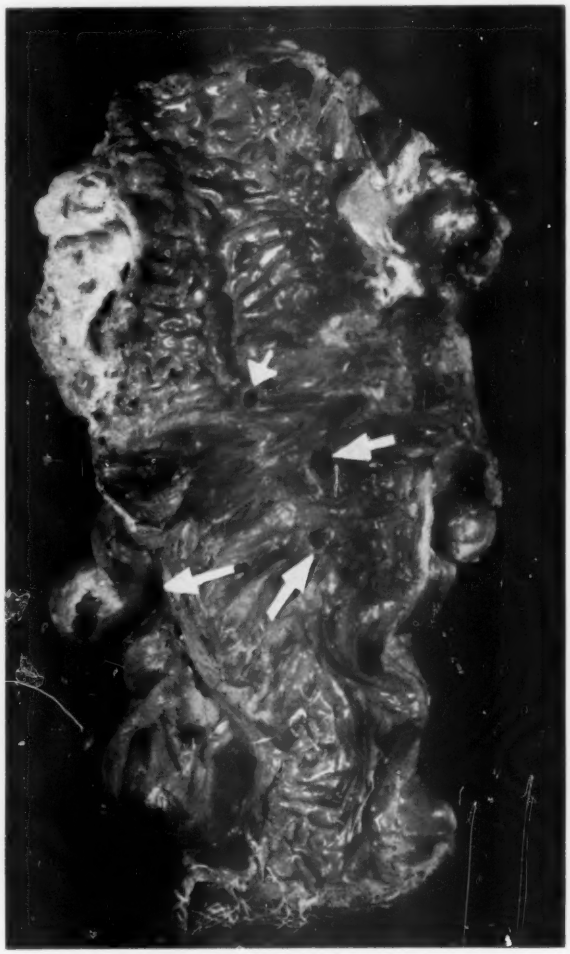

FIG. 5.—Acute sigmoiditis with multiple diverticula. Note thickness of inflamed wall. Resected because of suspicion of carcinoma. (Refer to the roentgenograms of the same case, Fig. 3.)

stool. There may be dilation of the cecum. Temperature and leukocytosis are absent unless a complication is present.

If the obstruction is acute, and apparently complete, prompt operation is indicated. It should usually be of a palliative nature and be limited to a cecostomy, colostomy or a first-stage Mikulicz procedure. A differential

diagnosis may be possible after the acute symptoms have subsided, and will influence the subsequent treatment.

In incomplete obstruction there is usually time for observation and diagnostic examinations, the same as in uncomplicated cases. If pain or tumor persists, or there is a suspicion of carcinoma, an exploratory operation is indicated. It does not always clarify the situation, and resection may have to be resorted to as a safety measure.

Treatment.—Of the 82 cases reported, 46, or 56 per cent, were uncomplicated. Patients with normal or very slight temperature were treated ambulatorily. They were put on a light diet, with little residue, and mineral oil was ordered for morning and evening. Rectal irrigations were given when indicated, and either a hot-water or an ice-bag applied during the resting periods.

All the more acute cases were put to bed. Aside from fluid diet, and perhaps a little mineral oil, nothing was ordered until a probable diagnosis could be made. A blood count was done. As soon as it was considered safe, a careful rectal irrigation was given. This was followed by roentgenologic examination, rarely after a barium meal, but usually after a barium clysma, which must be given carefully to avoid perforation. In one case severe pain followed a barium clysma given at a roentgenologist's office. The patient developed an abscess which was neglected and resulted fatally. With rest, perhaps the application of an ice-bag or heat, and with careful rectal irrigations, the acute symptoms usually subside in a few days and the patients become ambulatory. It is interesting to observe how quickly a large mass may disappear. In case there is unusual delay, the reason has to be looked for. In a few cases roentgenotherapy was apparently of value in aiding dissolution of the mass.

After the acute symptoms had subsided, patients were instructed in the pathology underlying their complaints. They were also made familiar with the measures calculated to avoid recurrence—such as the use of mineral oil to insure daily evacuation, restriction of food with a large residue, and avoidance of overeating. That these measures apparently have some success is evidenced by the fact that most patients have remained free from recurrence. On the other hand, several recurrences have shown that there is no positive safeguard in avoiding acute inflammation in those patients afflicted with diverticulosis. The condition must be considered a serious one, and one must be prepared at any time to see a recurrence or a complication requiring surgical intervention. In spite of definite instruction, two patients failed to apply for treatment promptly on the return of symptoms and were finally admitted with a neglected abscess to which they succumbed.

Surgical Treatment.—In the remaining 36, or 44 per cent, some type of surgical intervention was indicated or became imperative. In two of these, operation was not carried out. One of them was a patient with an associated carcinoma, who refused operation. The other one had general peritonitis

with multiple abscesses; she was admitted practically moribund and died within 24 hours.

This leaves 34, or 41.5 per cent, of the 82 cases in whom some type of operation was performed. Surgical treatment was always undertaken for a definite indication, either for perforation with abscess or peritonitis; for obstruction; for persistent pain; for recurrent attacks; or on the suspicion that carcinoma might be associated with the condition.

The procedures detailed in Table IV were carried out:

TABLE IV

OPERATIVE PROCEDURES

Total Cases Operated Upon 34, or 41.5%

Exploratory operation	3
Exploratory operation with separation of adhesions	4
Colostomy	6
Cecostomy	2
Resection	8
6 for inflammatory mass	
2 for carcinoma	

Acute Perforations 19, or 23.2%

With abscess	7
With peritonitis	12

Procedures Carried Out in This Group

Drainage only	14
Drainage and appendicectomy	3
Drainage and resection	1
Drainage and colostomy	1

The most serious cases were those with acute perforation. Some presented very complicated pictures with peritonitis; pus pockets; adhesions; obstruction; *etc.* In one case, an associated carcinoma had perforated. Loops of small intestines were adherent to the mass in some cases and produced obstruction by angulation. In one case there was thrombosis of the vessels with gangrene of the sigmoid.

Of the 12 cases of peritonitis that were operated upon, only four recovered completely. Six died at the hospital and two others recovered temporarily and died long after of complications or sequelae. One of these had an associated carcinoma.

Of the seven perforations who developed an abscess, five recovered and two died. In one of these neglected cases the abscess dissected retroperitoneally in spite of drainage and pointed in the opposite groin.

In the 15 cases operated upon for obstruction, persistent symptoms or tumor, or because of the suspicion of malignancy, the same rules which guide surgeons in colon surgery for other conditions were applied. In several cases a stage-operation, with preliminary cecostomy or colostomy, was performed.

The simplest operation was an exploratory celiotomy in three cases, and

combined with separation of adhesions in four others. The operations were undertaken for the relief of symptoms or to rule out carcinoma. In three of these patients, the tumor mass was lifted out of its bed where it had become adherent and produced incomplete obstruction, and placed into a more favorable location.

A cecostomy was performed on two cases for the relief of obstruction. In one case, it was closed after the acute symptoms subsided. In the other case, it was left permanently as a safety valve.

A colostomy was performed in two cases for the same reason. One case had an inoperable carcinoma associated with diverticulitis, while the other had complications which eventually led to a fatal outcome. Of the other four colostomies, three remained permanently, after resection of an inflammatory tumor. In only one case was it possible to close it later. This is due to the fact that the involved segment, which requires resection, is so long, that the ends of the remaining intestine cannot be approximated. The lower stump is simply closed and allowed to drop back. A combined abdominoperineal resection is not required in benign lesions.

Of the eight resections, two were performed for carcinoma—two for a painful, recurrent mass with inflammation or suppuration in the wall; and four, because the lesion was suspicious of carcinoma. All recovered from the operation. The carcinoma cases have since died, but the benign cases remained well.

Results.—The total, immediate mortality in the 34 cases operated upon was eight, or 23.5 per cent—restricted entirely to the acute perforations. There were, in addition, two late deaths from complications and four deaths due to carcinoma. One case died of carcinoma and one of peritonitis without operation. This makes a mortality rate of 19.5 per cent, or 16 mortalities out of the total 82 cases, which may be attributed directly to diverticulitis or one of its complications or associated conditions. By excluding the five carcinoma cases, the death rate is 13.4 per cent, or 11 mortalities with or without operation.

TABLE V

SUMMARY OF RESULTS

Total No. of Cases	82
Uncomplicated cases treated conservatively	48
Died as result of the disease	2
1 peritonitis	
1 carcinoma	
Complicated cases operated upon	34
Early deaths from perforation	8
Late deaths from complications	2
Died of carcinoma	4

Of the 20 operated cases who recovered, two have since died of intercurrent disease, 18 and 25 years after operation. This leaves 18 cases living at the present time. Fifteen are entirely well; one has a ventral hernia; one has

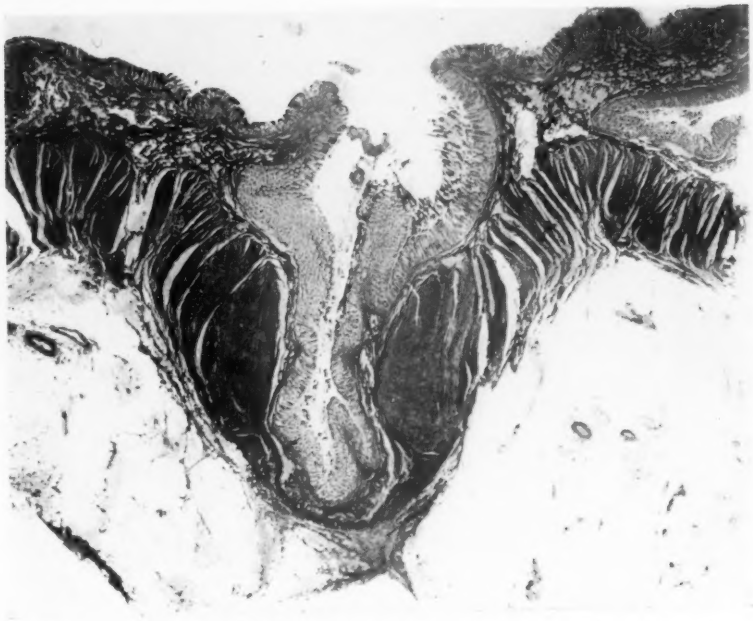

FIG. 6.—Diverticulum of sigmoid buried in wall. Does not project beyond serosa.

FIG. 7.—Complete diverticulum of the sigmoid projecting beyond the serosa.

a colostomy; and one has a fistula, which is of recent origin and will probably close shortly.

Pathology of Acute Sigmoiditis.—The mass seen and felt at operation, during an acute attack of diverticulitis, is a red, hard, nodular tumor. The appearance is due to thickening of the wall, involvement of the appendices epiploicae and diverticula, as well as adhesions. The serosa is rough and granular and frequently there is fibrin deposit and perhaps a small encapsulated abscess in the wall. This appearance usually permits dif-

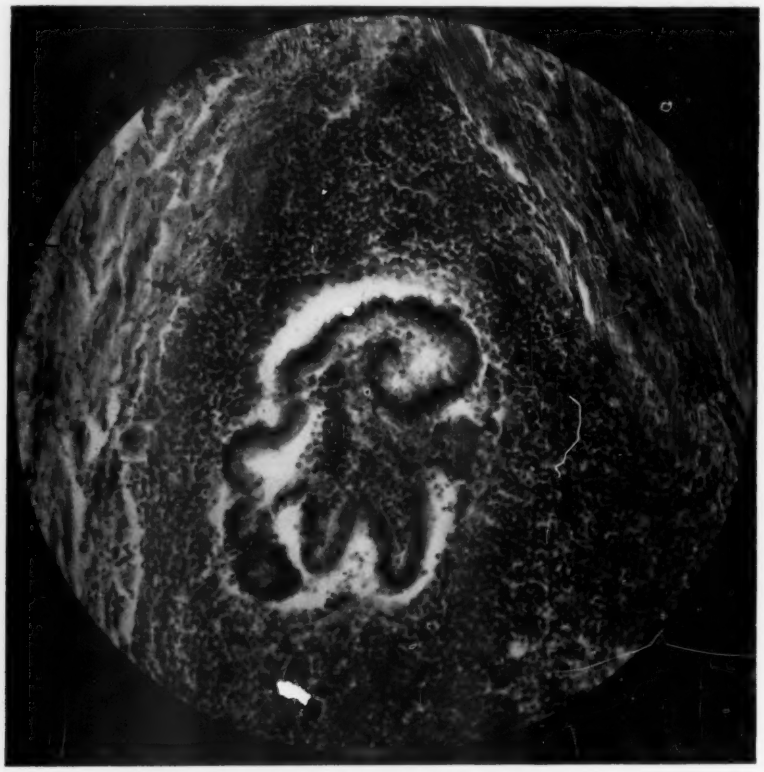

FIG. 8.—Diverticulum of sigmoid surrounded by round cell infiltration.

ferentiation between an inflammatory mass and carcinoma. If peritonitis is present, indicating that perforation has most likely taken place, careful search frequently fails to reveal any opening. One may assume that it was of pin-hole-size only and has become closed off with a fibrin plug, or that bacteria have passed through the wall and involved the peritoneum. Whether to resect or not under these circumstances is a question of judgment.

Without gross perforation or exudate, perhaps, in a case diagnosed as appendicitis or sigmoiditis, we have simply removed the appendix and closed the abdomen. If exudate was present, we have drained. In several cases in which the tumor mass had dropped into the pelvis, angulated the sigmoid, and had loops of small intestine adherent to it, we have freed the adhesions,

lifted the tumor out of its bed and placed it into a more favorable position. The results have been very satisfactory.

In case a gross perforation is present, the involved intestine should be exteriorized by a Mickulicz procedure, if that is possible, and later resected. If that is not possible, because of fixation or length of involved segment, ample drainage and a colostomy above the lesion is the procedure of choice. If the exudate due to perforation has been walled off to form an abscess, early and adequate drainage is essential because of the danger of rapidly spreading putrid infection.

In case resection is performed, and the specimen is opened, it is surprising how little actual obstruction exists. The mucosa is either normal or it shows

FIG. 9.—Cross-section of colon. The larger lumen is that of the intestine. Above it is an acute abscess (in a diverticulum), the walls of which are partially lined by intestinal mucosa. The remaining portions of the mucosa have been destroyed by the suppurative process.

redness and superficial erosions, but no ulceration. It is at once evident that the lesion does not arise in the mucous membrane as in carcinoma, but is confined to the wall and perisigmoid tissues. Openings of one or several diverticula may be visible and pressure on the thickened wall will cause exudation of secretion or expulsion of small hard fecoliths which had been impacted in the diverticula (Fig. 5).

Studying the thick edematous wall of such a resected specimen frequently reveals no definite diverticula visible externally. They may be in an early stage of development, still confined within the wall as shown in Figure 6. Even in this state however, they may become inflamed and, by perforation into the wall, produce a phlegmon which, in turn, produces the tumor mass. An inflamed, fully developed diverticulum is more likely to perforate externally and give rise to peritonitis (Fig. 7).

Microscopic study of resected specimens shows diverticulitis or sigmoiditis, with small round cell infiltration surrounding the diverticula (Fig. 8), or an acute suppurative process (Fig. 9). In five of our cases there was an asso-

ciated carcinoma. Whether this condition is an independent lesion or whether it is the result of irritation produced by the diverticulitis, is left to conjecture.

SUMMARY

(1) A group of 82, personally observed, cases of acute sigmoiditis and diverticulitis is reported.

(2) The majority of cases recover with conservative treatment and they may guard against recurrence by regulation of diet and bowel habits.

(3) In this series of carefully followed cases, 36 patients, or 43.9 per cent, developed a condition which seriously threatened their lives.

(4) Twenty of these, or 24.4 per cent of the total, developed acute perforation with abscess formation or peritonitis. In 14, a simple drainage operation was performed; in five others drainage plus some other procedure, and one was not operated upon. There was a mortality of nine early deaths, or 45 per cent. There was one late death from complications—making a total mortality of ten cases, or 50 per cent directly due to perforation.

(5) Twenty-three other operations were performed, either an exploratory celiotomy, exploratory with separation of adhesions, colostomy, cecostomy, or resection. There was no mortality in this group.

(6) There were five patients with an associated carcinoma, all of whom eventually succumbed to the condition.

(7) The total mortality, directly traceable to the sigmoid lesion, was 16, or 19.5 per cent.

(8) The pathology is described.

(9) This group-study of acute sigmoiditis and diverticulitis calls attention to the seriousness of the condition. It reveals that diverticulosis, as such, is not an innocuous lesion. Once recognized in a patient, the physician or surgeon assumes a serious responsibility if he allows the patient to depart without warning him of possible danger and instructing him in the known means at our command to avoid complications.

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DISCUSSION: DR. JOHN E. JENNINGS (Brooklyn) asked if Doctor Eggers would explain the difference in mortality of the operated and nonoperated cases. He pointed out that the nonoperated cases seemed to show a higher survival than those that were operated upon, and said that this corresponded to his own experience. He also said that he had noted that acute, fulminating cases of diverticulitis have been more often left-sided than right-sided, and that these cases are often erroneously diagnosed as ruptured appendices that

had abscessed. One should avoid, insofar as possible, the brusque invasion of the left abdomen.

Dr. Carl Eggers (New York) in closing stated that he was a firm believer in conservative treatment, and that operation should be reserved for cases with persistent symptoms, complications, or associated lesions. These include perforation, obstruction and carcinoma. Some of the patients in Doctor Eggers' series were operated upon under the mistaken diagnosis of acute appendicitis, others were acute surgical emergencies with peritonitis or abscess. Of the 12 perforations with peritonitis which were operated upon, four recovered completely, six died in the hospital, and two succumbed a long time after operation as the result of complications. Of the seven perforations with abscess, five recovered and two died. In one of these, the abscess dissected retroperitoneally and pointed in the opposite groin. The total immediate mortality in the 34 cases operated upon was 23.5 per cent, and was restricted entirely to acute perforations. There was no mortality in any of the operations of choice. The total mortality was 19.5 per cent, including five carcinoma cases. Deducting these, the death rate was 13.4 per cent, with or without operation.

LYMPHOGRANULOMA VENEREUM*

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The present status of lymphogranuloma venereum has evolved, through many years of clinical study, from a disease of the external genitals associated with inguinal and rectal lymphogranulomata. It came to be realized that the disease was not syphilis, gonorrhea or chancroid but may be associated with any one or all of them, and possessed a specificity for the Frei test.[1] †

Since 1930, lymphogranuloma inguinale has received particular attention in the American literature. Clinical cases are now recognized and hospitalized in increasing numbers in the wards of hospitals in the larger cities. At Bellevue Hospital (Third Surgical Division) lymphogranuloma inguinale appears in the files for the first time in 1934.‡

A. Stillman,[2] J. Morris,[3] and R. Colp[4] have made contributions before the New York Surgical Society. Stillman, in 1934, reported on the advantages of colostomy, Morris, in 1938, showed an excellent result from abdomino-perineal resection of the rectum and the rectosigmoid, and Colp, in 1939, exhibited a case upon whom he had performed an abdomino-endo-anal resection of rectum and rectosigmoid.

Venereal lymphogranuloma, caused by an ultramicroscopic bacterium, may be regarded at present as a bacteriemia. It is transmitted through contact and has been recognized on the tongue[5] and on the surgeon's finger,[6] but predominantly on the external genitalia. The Frei test is positive after two to nine days[7] of incubation. Three days to three weeks after exposure, a primary sore appears on the genitals.[8, 9] This disappears in five to ten days[9] and is followed by inguinal node involvement in the male, rarely in the female. The skin over the nodes is purplish. Chills, fever, and night sweats appear with the perilymphadenitis. There are leukocytosis, relative mononucleosis, and eosinophilia.[9] Abscesses and sinuses appear in the groins and a thick, creamy-yellow, later, sanguineous pus exudes. As the chronic stage develops there occur elephantiasis of the vulva, penis, and scrotum, and rectovaginal thickening. The general surgeon is particularly concerned with the chronic stage and with the ulcerative stenosing proctocolitis that ensues. The patient com-

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† D'Aunoy and von Haam estimate the diagnostic error of the Frei reaction at less than 10 per cent on the basis of a two-year study of 1,697 examinations. Positive Wassermann reactions were present in 19.5 per cent of positive Frei cases; acute gonorrheal and chancroidal infections in 10 per cent (Am. Jour. Clin. Path., Baltimore, **6**, 529, 1936).

‡ At the present time, it is the practice on this division to have Frei tests on all inflammatory rectal cases and all problem cases with abdominal pathology.

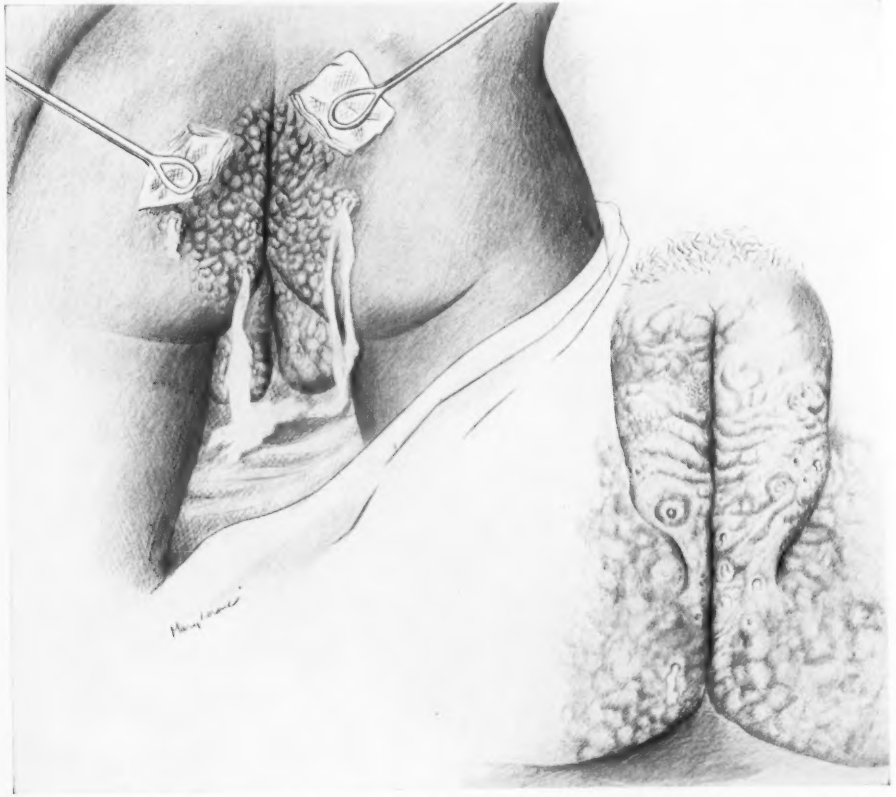


FIG. 1.—Drawing illustrating elephantiasis of vulva and perineum. Note sinuses and fistulae.

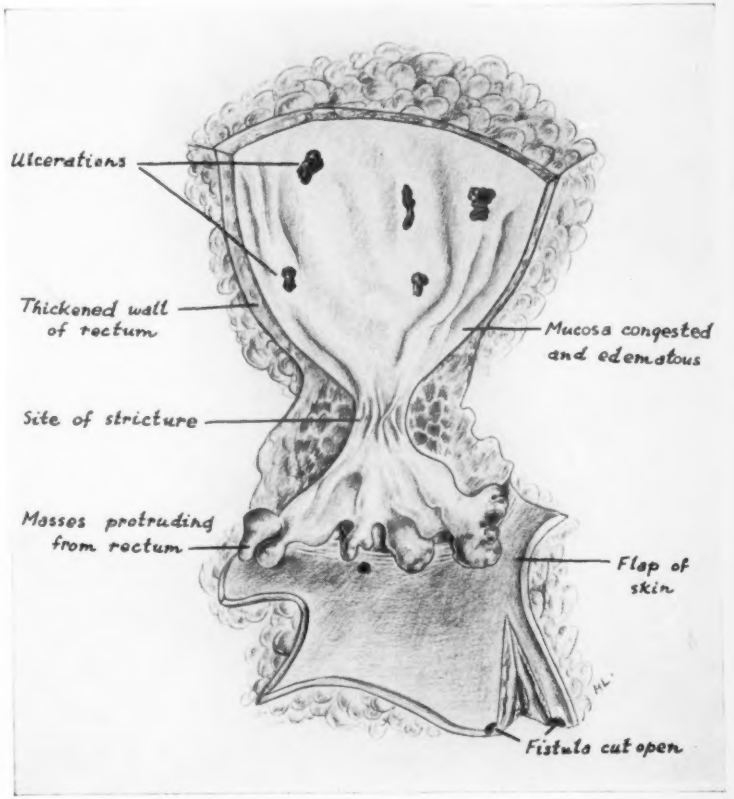


FIG. 2.—Lymphogranuloma. Drawing representing perirectal thickening and stenosis, fistulae, and ulcerations.

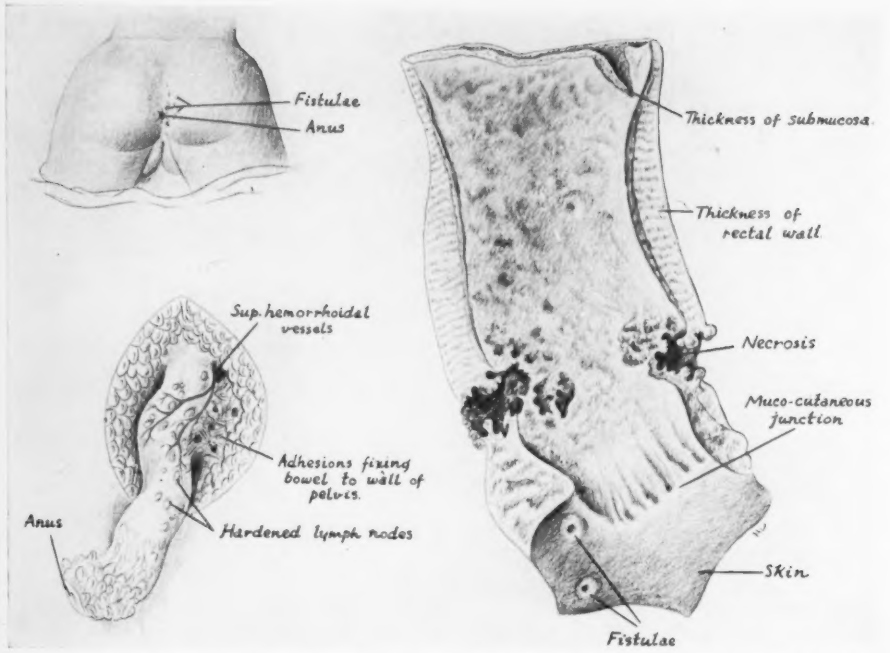


FIG. 3.—Lymphogranuloma Venereum. Drawing illustrating rectal fistulae, in upper left. Perirectal thickening and necrotic areas to the right of mesorectum and enlarged discrete nodes about superior hemorrhoidal artery, in lower left. To the right, the specimen is represented. Note especially extensive necrosis in lower rectal wall and marked thickening above.

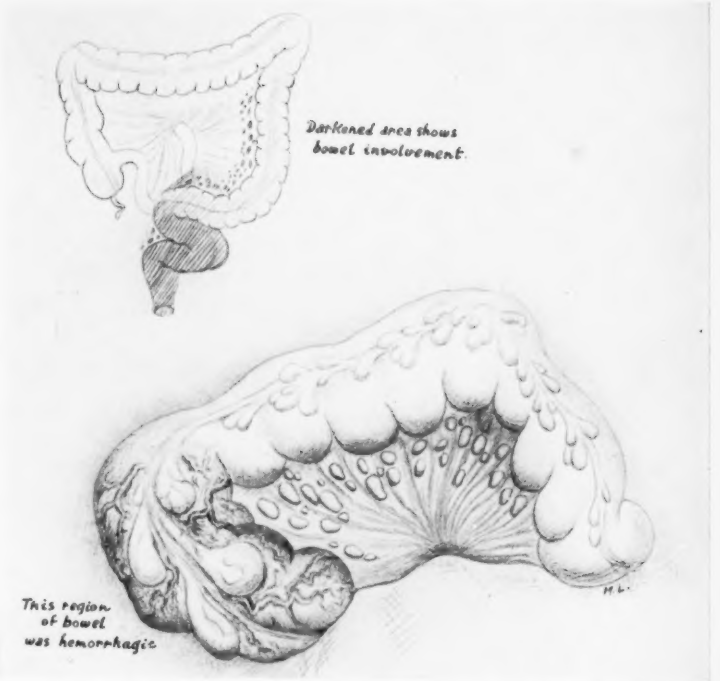


FIG. 5.—Extensive Lymph Node Metastases. One of the lymphogranulomata complicated by adenocarcinoma of the rectosigmoid. Note enlarged nodes in mesosigmoid and retrocolic tissue extending to region of splenic flexure.

plains at this time of pain and purosanguineous discharge from the rectum, inability to move the bowels, and general debility and asthenia.

The present review comprises 55 cases admitted on the surgical wards of the Third Division. It does not consider those treated on the nonsurgical wards. Of these 55 cases, 35 underwent resection of the rectum and variable amounts of sigmoid colon. These latter constitute the basis for this paper.

The average age of the total cases was 36.5 years, the oldest being 68, the youngest 20. There were 16 males and 35 females. Forty-three were Negroes and 18 Caucasians. The mean duration of the perineal symptoms was 3 years in 42 cases and 4.2 years for 18 of the resected cases. Lymphogranuloma venereum attacks all ages and is distributed throughout the world. Any reported statistics must vary with the population affected. The present data are characteristically both metropolitan and of a low social order.

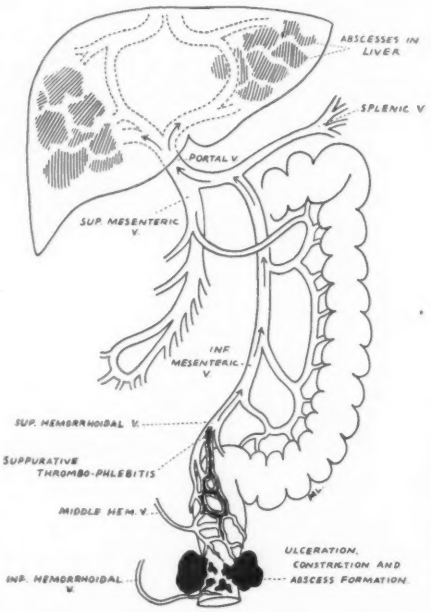


FIG. 4.—Diagrammatic drawing representing active granulomatous process in rectum and occasional means of spread through superior hemorrhoidal vein and portal system to liver. Necropsy revealed abscesses in liver as indicated.

The infectious process is essentially lymphatic in its spread. It enters the lymphatics accompanying the inferior, middle, and superior hemorrhoidal arteries. So many of the patients observed by us are females in whom the initial lesion is generally so high in the vaginal vault that only an occasional patient presented enlarged inguinal nodes. But there were sites of maximum damage and repair in the lower rectum, within a finger's length of the mucocutaneous junction and contiguous with the posterior vaginal wall. Here, stenotic scar or perforating ulcers occurred. Many of these ulcers communicated with the vagina. In an occasional case the perforation extended completely about the rectal wall so as to separate the anorectum from the upper rectum. The perirectal tissues supplied by the middle hemorrhoidal lymphatics appear to be next seriously involved and for some unknown reason those on the right side more than those on the left. Fan-shaped masses of fibrotic tissue interspersed with necrotic foci, evidently disintegrated lymph nodes, were observed to point from the lateral walls of the midrectum beneath the deep fascia and close to the periosteal surfaces of the floor of the true pelvis. When these "fixating" shafts of inflammatory tissue were divided in the course of rectal dissection, one or more sinuses appeared. In addition to these sinuses or blind fistulae several external fistulae proceeded from the rectum and discharged externally on the surface of the

perineum, as represented in Figures 1, 2 and 3, and described in the pathologic findings. Finally, the pararectal and mesorectal fat and lymphatics, at the level of the superior hemorrhoidal arteries, were demonstrably involved but to a lesser extent than those of the middle and inferior hemorrhoidals. There were edema and hyperplastic nodes. The extent of the lymphadenitis within the abdomen varied from barely palpable nodes in the presacral area to the general enlargement of the retrocolic nodes of the sigmoid and descending colons.

In the extreme case these stages of lymphatic involvement are not recognizable but the whole rectum, posterior vaginal wall, and pararectal and presacral tissues are generally necrotic and suppurative. The infection has spread on into the abdomen and the general condition is so depleted that exitus is imminent whether dependent pelvic drainage is attempted or not.

Another means of dissemination, which is less frequent, is that by way of the superior hemorrhoidal and pelvic veins. This was well illustrated in an autopsy performed on an advanced case. Figure 4 shows the thrombophlebitis of the inferior mesenteric vein and the multiple intrahepatic abscesses found in this instance. In a few of the cases perihepatic adhesions and peripherally scarred livers were observed in the open abdomen. It was thought that bacteriemia existed in the portal circulation and was taken care of by the liver even at the expense of liver damage. Where the infection broke through into the general circulation, and positive cultures were obtained, the patients were too acute for operation.

In addition to the involvement of lymphatics and veins arising from the site of original contamination the mucosa of the anorectum, sigmoid, and rarely the descending colon showed inflammation, most often ulcerative. It is not known whether this ulcerative colitis was due to the lymphogranuloma virus or to a secondary infection. The ulcers are quite generally regarded as nonspecific. Many colonic ulcers occur with relatively minor pathologic changes in the rectum. All the cases but two, of the 35 resections, were associated with a positive Frei test.

The pathology in this group of malignant inflammations of the rectum is strikingly similar and in no way specific. Thirty-five specimens were examined. In 33 of these the Frei test was positive. In these the change was a chronic productive inflammation with marked fibrosis and with small focal abscesses. Stricture was present in all, starting at a point immediately above the internal sphincter and extending for variable lengths up to the rectum and colon. In 30 cases the lesion was below the peritoneal reflection, usually being confined to the lower 12 cm. Two cases showed involvement of the sigmoid and descending colon. Both of these had had colostomies, the stomata of which were closed by extension of the inflammatory process.

In 26 cases the anal and perianal skin was involved, 22 showing one or more fistulous openings. In one case there were eight separate external openings. In six cases there was no involvement of the sphincters or perianal tissue.

Annular ulceration of the mucosa was uniformly present, extending the entire length of the stenosis. The degree of stricture varied. In ten cases the rectal lumen appeared as a tortuous canal, in places measuring less than 0.5 cm. across. In the other 25 cases the stricture was not as marked.

Microscopic examination showed complete loss of mucosa with a superficial slough composed of disintegrating tissue cells and pus. Beneath this there was a basic framework of new fibroblasts and new blood vessels with a heavy infiltration of lymphocytes and plasma cells. Occasional small abscesses were present. Deeper in, the tissue fibrosis was more marked, cellular infiltration less dense and there was a tendency toward perivascular infiltration. Fewer abscesses were seen. The reaction appeared less active than that near the lumen. Throughout the tissue multinuclear giant cells of the "foreign body" type were seen. At the upper limits of the lesion the inflammatory reaction had extended well beyond the area of ulceration. Here the reaction was most marked in the submucosa with a perivascular reaction in the muscle layers.

Two cases showed carcinoma, one, squamous cell, involving the mucocutaneous junction at the level of the internal sphincter, and the other, an adenocarcinoma, involving the ampulla of the rectum.

Two cases had a negative Frei test. In both, the inflammatory process was confined to the anal canal, perianal tissue and lower 6 cm. of the rectum. The skin about the anus was thrown into condylomatous formations with multiple sinuses leading toward the rectum. There was dense infiltration of lymphocytes and plasma cells in the epidermis, dermis and subcutaneous tissue. Histologically, this lesion appeared identical with those previously described. In one of these cases a positive clinical diagnosis of granuloma inguinale had been made.

The complications included five cases of arthritis or an incidence of 9 per cent in these surgical lymphogranulomata, which is far greater than 1.6 per cent of 186 cases from the Dermatologic Service for a corresponding period. McEwen[10] found no permanent damage in these joints. From his studies in these cases he was inclined to regard them as a definite manifestation of lymphogranuloma venereum.

Carcinoma followed the rectal granulomata in three of the 35 resected cases* (Fig. 5). Five of the operated cases were psychotic. Unless the progress of the infection is checked they become profoundly prostrated and die of sheer exhaustion, go on to complete obstruction, peritonitis, meningitis,† or general sepsis.‡

* Since the preparation of the present communication, four additional resections, including one for complicating carcinoma, bring the incidence of malignancy associated with lymphogranuloma venereum to 8.6 per cent. Also ref. David, V. C., and Loring, M., *et al.* ANNALS OF SURGERY, **109**, No. 5, 837–843, May, 1939.

† The virus of venereal lymphogranuloma seemingly has a special affinity for the nervous tissues. (Pisacane, C., and Lopresti, R.: Riforma Medica, Naples, **55**, 332, March 4, 1939; also Levy-Valensi and Seze, S. de: Presse Medicale, Paris, **47**, 593, April 19, 1939.)

‡ See opposite page.

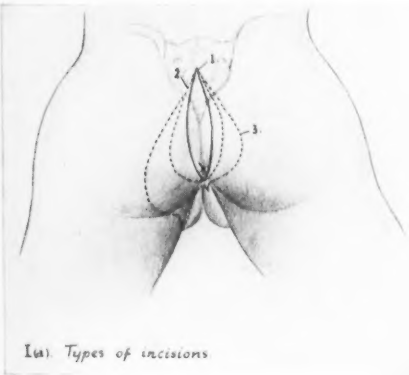
The prognosis, therefore, is bad for the case refractory to palliative therapy unless operated upon. Of these surgical cases the prognosis is not good in the presence of nodular enlargement above the sigmoid colon or with gross liver pathology or with bacteriemia or meningeal symptoms.

The treatment was necessarily surgical in all these cases, as medical treatment, including chemotherapy and vaccines, had long been tried and had failed. The paramount indication was taken to be drainage. There was so much massive suppuration and necrosis in and about the anus, rectum, and sigmoid that nothing short of resection of the rectum, to, and including the rectosigmoid junction and the grossly infected necrotizing pararectal tissues, could effect satisfactory drainage. Palliative operations for hemorrhoids, fistulae, and strictures were performed on the early cases but always with the understanding, in the Frei positive cases, that the process would progress and require surgical excision at a later date. There is no question that colostomy alone is helpful in lymphogranuloma.* Between the stages in the present series definite improvement in the ulcerative colitis and a partial clean-up of the perineal suppuration were repeatedly observed. But on the other hand the infection buried in the pelvic lymphatics and fascial planes behind and below the peritoneum is allowed to smolder, increase, and be absorbed. Such patients have pain and discharge, become toxic and asthenic. Patients colostomized, elsewhere, have applied for assistance too prostrated for any further surgery. In two of these the original colostomy ceased to function as the granulomatous process had crept up to, and involved, the sigmoidostomy stoma. One such case was admitted to die of intestinal obstruction. It is true that no procedure can help many of these wretched people but it is encouraging to observe the striking improvement in the great majority of our patients in the short time in which they have been followed.

It is surprising, and seemingly contrary to general surgical experience, to observe the rapid healing of these contaminated sacroperineal wounds. We are aware that all fistulous tracts are not always primarily removed in their entirety. Many cases continue to drain for several weeks. Subsequent incisions, during the process of healing, expose the source of reinfection and

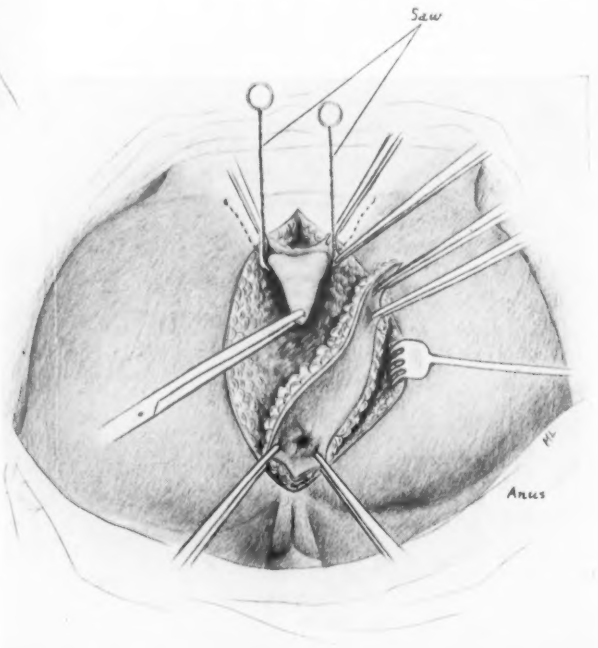
‡ In two of the five hospital deaths *Streptococcus haemolyticus* was recovered from the blood several days antemortem. We are inclined to believe, at the present writing, that the various micro-organisms recorded as having been obtained from the blood and spinal fluid, joints and peritoneum, and from the intestinal mucosa are secondary invaders which have naturally followed in the wake of a lowering resistance produced by the etiologic agent of this disease. It may be significant that the intestinal nodes uniformly react—reach a certain size (not over 1–1.5 cm.) and consistency and remain discrete, then necrose, whether presacral or retrocolic. These are quite different from those met with in the groins during the acute stage of mixed infections or in the regional metastases of carcinoma. Possibly, future studies of this unknown causative factor along biologic lines, in addition to the routine clinical and bacteriologic methods, may throw more light upon it.

* Compare the experience of H. W. Cave with chronic ulcerative colitis. (J.A.M.A., **113**, No. 7, 551, August 12, 1939.



I(a). Types of incisions

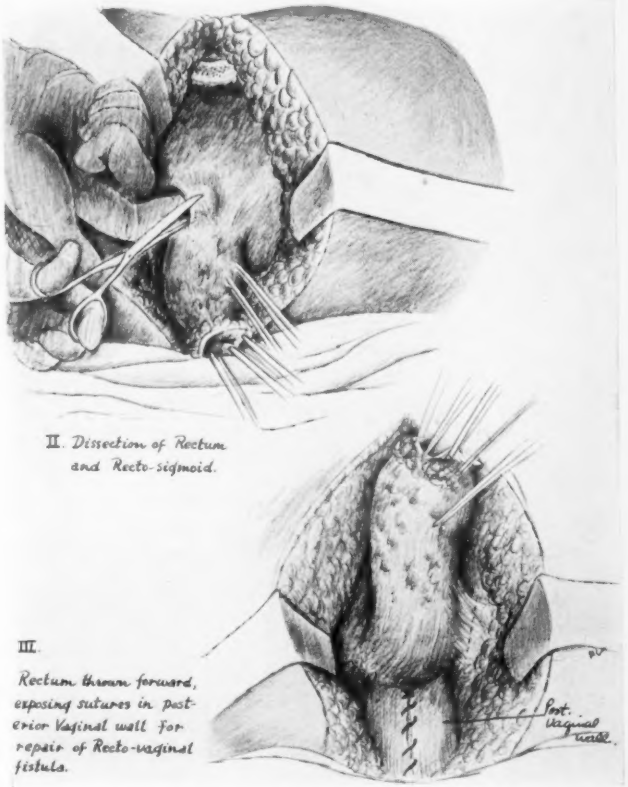
Coccyx and lower sacrum. (Rest of sacrum in dotted line



I(b) Incision and removal of Coccyx and lower sacrum

FIG. I(a).—The incision is carried from the third sacral vertebra downwards about anus so as to include the perirectal inflammatory tissue and fistulous tracts.

FIG. I(b).—The skin flap is mobilized. Anal opening is closed by suture or by clamping together edges of detached skin over it to prevent soiling of wound. Coccyx and lower sacrum are removed to afford a free approach to the presacral tissues and rectosigmoid.



II. Dissection of Rectum and Recto-sigmoid.

III.

Rectum thrown forward, exposing sutures in posterior Vaginal wall for repair of Recto-vaginal fistula.

Post. vaginal wall

FIG. II.—The rectum is being mobilized after division of levatores ani and dissection of perirectal fasciae.

FIG. III.—The rectum is brought upwards to facilitate repair of the posterior vaginal wall for rectal fistula.

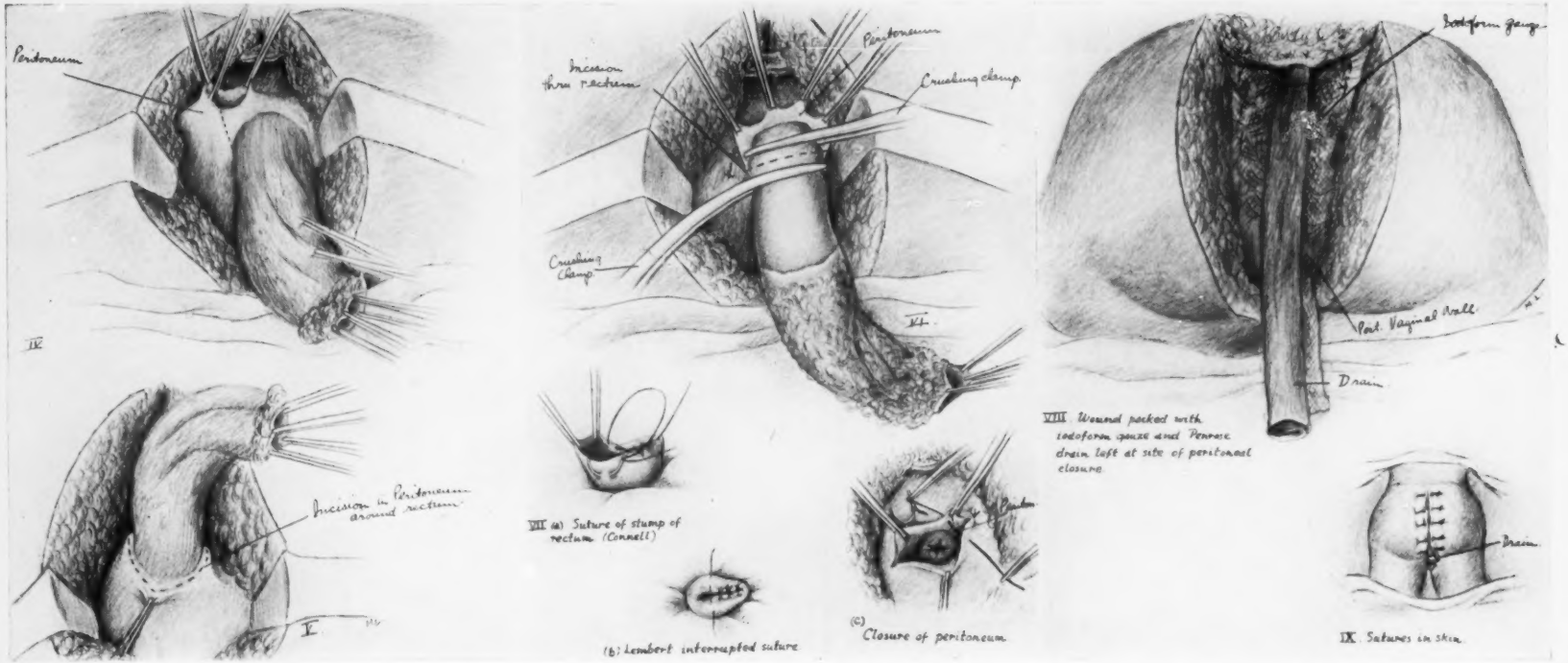


FIG. IV.—The rectum is drawn downwards, exposing the rectal peritoneal relations.

FIG. V.—The rectum is elevated, disclosing the line of incision in the peritoneum about the rectal wall.

FIG. VI.—The rectum and the lower portion of the pelvic colon are delivered after freeing the peritoneal and mesorectal attachments.

FIG. VII(a), (b), and (c) show the successive steps in the treatment of the proximal stump of the pelvic colon and the closure of the peritoneum underlying it.

FIG. VIII.—The wound is prepared for suturing. Note the drains at the site of the peritoneal closure carried out through the lower angle of the wound.

FIG. IX.—The skin and the soft parts are approximated by a single layer of interrupted sutures.

maintain the drainage. One of these patients returned to our wards with a diagnosis of malignancy from another hospital, but subsided after ample pelvic drainage was reestablished. Another case generally improved in weight and well-being presented a continuously necrotic discharge at the upper posterior extremity of the wound. Repeated incisions, finally carried into the third lumbar intervertebral region, and prolonged open drainage were followed by complete healing. Although roentgenograms were negative, there were bony grating and probably superficial osteoperiostitis. This was believed to demonstrate, more strikingly than in the pelvis, the burrowing of the lymphogranulomatous process into the soft parts and the resistance of bone.[11] One feels that there is certain virtue in uncovering these concealed infectious pathways and letting in air and light. With the exception of these occasional cases, with deeply concealed and inaccessible sinuses, the convalescence has been very encouraging. Sacroperineal resection, leaving a sacral anus, was performed in four of the earlier cases. It was soon realized that it was impossible to determine the degree of sigmoidal involvement without celiotomy. To avoid subsequent colostomies at a higher plane, all subsequent cases were celiotomized. Colostomy was performed about ten days prior to resection. It was fashioned after Mikulicz in those (three cases) in whom some hope remained of restoring the perineal route or of preserving the natural anus. A permanent abdominal anus was made in the advanced cases. Twenty-eight of these cases were of this latter category.

We have come to the conclusion with Lynch,[12] and others, that posterior resection above the anal sphincter is unwise. The firm cartilage-like scar following terminal anastomosis is, in our experience, about as troublesome as the original stricture. And denervation of the sphincter seems to further interfere with satisfactory function. We prefer to leave certain of these patients, and those who require it, with artificial sacral ani. Unless the formation of a sacral anus was effected at the time of the sacroperineal resection none was created at all for no changes from an abdominal to a sacral anus has subsequently been made in this series. Whether left with a sacral or an abdominal left rectus colostomy, the patient is taught, by the charge nurse, the care of the bowel and is instructed in the diet so that the patient is prepared to continue the new hygiene at home.*

No artificial bags of any kind are advised. Simple cleanliness, kaolin, and dry gauze make up the essentials of the colostomy dressings.

These patients generally improve in morale, in body weight, and return to habits of living similar to those enjoyed before the onset of the disease.

With the exception of five extreme cases all the remainder of the 35 resections survived. This gives an hospital mortality of 14.3 per cent. There were no immediate postoperative deaths.

* The authors wish to take this occasion to express their sincere appreciation for the faithful and self-sacrificing attention given these patients by Miss Katherine Gannon, R.N., and her associates.

SUMMARY

(1) Lymphogranuloma venereum has been reviewed as presented on the Third Surgical (N.Y.U.) Division, Bellevue Hospital, 1936–1939.

(2) The total observed included a few direct admissions under some other classification but was largely made up of transfers from the Dermatologic, Medical, and Gynecologic wards in the hospital.

(3) The surgical treatment was radical for the obstructed case and palliative for the inflamed but nonobstructed one.

(4) Of 35 resections, four were one-stage sacroperineal and 31 were abdominal colostomies followed by sacroperineal resections.

(5) The hospital mortality was 14.3 per cent.

(6) The convalescence in the uncomplicated case was remarkably favorable.

The authors gratefully acknowledge the cooperation of Drs. Arthur M. Wright and Douglas Symmers, of Drs. F. M. Harrison, J. Lawler, J. Croce and the other members of the Third Surgical Division, Bellevue Hospital; and the expert technical assistance of Miss Mary Lorenc.

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A GASTRIC SECRETORY DEPRESSANT IN EXTRACTS OF ACHLORHYDRIC CARCINOMATOUS STOMACHS*

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A PLAUSIBLE HYPOTHESIS to explain the inhibited gastric secretion and achlorhydria in certain carcinomatous stomachs is that some gastric secretory inhibitor is elaborated either as a factor associated with pathologic conditions which precede or accompany the development of the neoplasms or as a factor identified with an hyperactive normal mechanism for inhibition of gastric secretion. Such an hypothesis has been mentioned at times in the literature[1] but has not been studied experimentally except for a report by Brunschwig, J. van Prohaska and Clarke.[2] These authors injected achlorhydric gastric juices from patients with carcinoma of the stomach into dogs with gastric fundus pouches which had been stimulated by feeding, and observed a transitory marked inhibition of volume of secretion and achlorhydria in 78 per cent of the 27 samples tested as compared with approximately 20 per cent in controls. Similar results were obtained using achlorhydric juices from patients with pernicious anemia.[3]

The method of studying factors which might influence gastric secretion by the intravenous injection of the substance to be tested into gastric-pouched dogs is a classic mode of experimentation in gastric physiology. As in the previous studies with gastric juices, such animals were employed in the following experiments, but instead of injection of gastric juices extracts of carcinomatous stomachs were employed.

Preparation of Extracts.—In the original work of Edkins[4] 0.2 per cent HCl extracts of gastric mucosa, when injected intravenously, were observed to stimulate gastric secretion in an anesthetized animal. This stimulating factor was called "gastrin." Since his publications in 1910, the existence of "gastrin," as a substance apart from histamine, has been the subject of controversy, but it would appear from the recent report of Komarov[5] that "gastrin" and histamine are not identical. In the following studies, Edkin's

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This work was conducted under grants from the International Cancer Research Foundation, Philadelphia, Pa., and from the National Advisory Council on Cancer of the U. S. Public Health Service, Washington, D. C.

† Research Assistants, International Cancer Research Foundation Grants.

method of extraction was followed. It was felt that if clinically, under stimulus by histamine, the human carcinomatous stomachs were achlorhydric, a secretory depressant action observed with extracts obtained by the technic employed to recover a gastric secretory stimulant, would perhaps be of greater significance than if another method of extraction were employed.

Thus, in carcinomatous stomachs removed at necropsy in the Department of Pathology of the University of Chicago, or partially resected at operation, the mucosa was stripped from the muscularis, cut into small pieces and ground

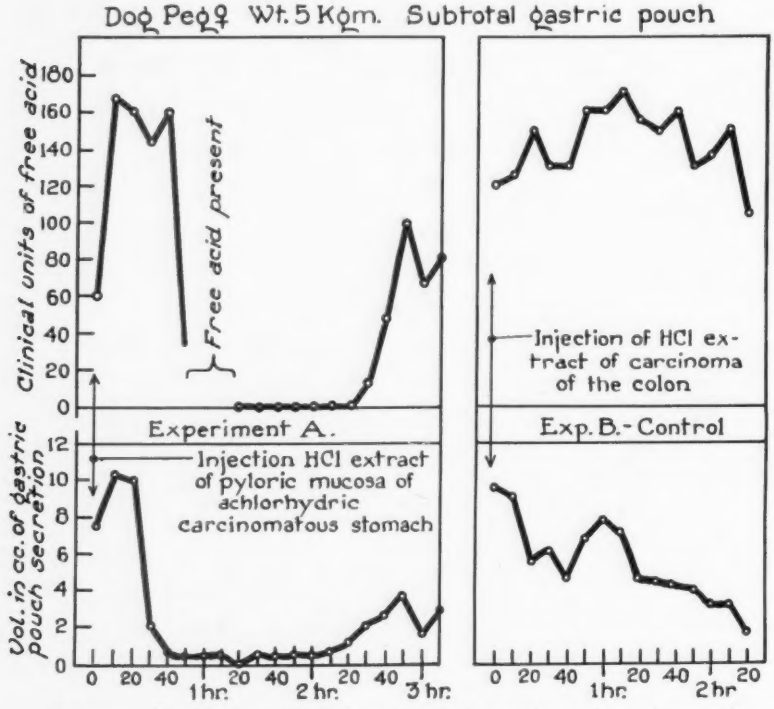
Dog Peg ♀ Wt. 5 Kgm. Subtotal gastric pouch
Clinical units of free acid
Free acid present
Injection of HCl extract of carcinoma of the colon
Experiment A.
Exp. B.- Control
Injection HCl extract of pyloric mucosa of achlorhydric carcinomatous stomach
Vol. in cc. of gastric pouch secretion
1 hr.
2 hr.
3 hr.

CHART 1.—Showing suppression of gastric pouch secretion and transitory achlorhydria due to injection of 0.2 per cent HCl extract of pyloric mucosa of an achlorhydric carcinomatous stomach. Graphs of a control experiment, in which acid extract of a carcinoma of the colon was employed, are also shown. In each of these experiments the animal was given one large feeding at the beginning of the experiment and no subsequent feedings.

in a mortar with sand. Two-tenths per cent HCl, or distilled water, was added in proportion of 50 cc. per 12 grams of tissue. The mixture was boiled in a Kjeldahl flask for ten minutes, allowed to stand overnight at room temperature, centrifuged, the supernatant cloudy fluid decanted and neutralized to litmus with NaOH. Distilled water was added to make up to original volume. Upon neutralization, a flocculent precipitate developed. The extracts were stored in an oven kept at 56° C. Before use, the extracts were shaken to obtain a uniform dispersion of the precipitate.

As a rule, the carcinoma was grossly resected from the stomach and extracted separately. However, histologic studies showed that the growth

had practically always extended beyond the gross limits into the surrounding mucosa and that extracts of mucosa could not, therefore, be regarded as free from material from the neoplasm. Thus, results using either mucosa or tumor are tabulated together.

Method of Experiment.—The dogs with gastric pouches were placed upon a large table, allowing freedom of motion and access to water. Soxlet flasks were suspended beneath the cannulae. Pieces of lean cooked meat were fed at ten- to 20-minute intervals, throughout the periods of observation. When vigorous acid secretion from the cannulae became established, the samples were collected at ten-minute intervals, the volume recorded, and titrated for free and combined acid, using 10/N NaOH and Töpfer's reagent and phenophthalein as indicators, respectively.

The extract to be employed was then injected in proportion of 1 cc. per kilo body weight (arbitrary dose). The animals were observed for at least two hours when no depression of pouch secretion occurred, and until free acid returned if a period of achlorhydria did develop.

Frequent rectal temperatures were recorded since in "fresh" animals a rise in temperature to above 40.5° to 40.6° C. was sufficient to produce suppression of secretion and achlorhydria on a thermal basis alone. Where such temperatures occurred the experimental results were discarded and the animal "immunized" to fever-producing substances in the extracts by repeated daily injections of small doses of the extracts. In some instances, temperatures above 40.5° C. always occurred but the gastric secretory mechanism became "heat resistant." Such dogs could be used once this stage was reached. In some such animals acid-pouch secretion was observed to continue even though the temperature reached 42° C.

Inhibition of pouch secretion and liberation of free acid followed the injection of some extracts from carcinomatous stomachs and some controls. The latent period for this varied from 30 to 70 minutes and occasionally was 100 to 120 minutes. A reduction in secretion volume to four drops or less for at least two ten-minute periods with persistence of free acid was regarded as significant and recorded as a +-result. Reduction in free acidity to 25 clinical units, or less, where the preinjection concentration of free acid was 60 or more clinical units was also considered a +-result. Reductions of free acidity from higher levels to 40 or 50 clinical units were not regarded as significant. Actual achlorhydria lasting ten to 30 minutes was recorded as a ++-result; achlorhydria lasting 30 to 60 minutes was considered as a +++-result; and achlorhydria lasting for 60 or more minutes was regarded as a ++++-result.

In biologic experiments of this type, where crude test extracts are used and where a number of known and unknown factors contribute to vary the conditions of each experiment, a variation in results is to be expected. Consequently, arbitrary criteria were established for the recording of results. For example, at least three different dogs (and often more) were employed to test a given extract, and an attempt made to perform at least five separate

experiments with a given sample. An extract from an achlorhydric carcinomatous stomach was not tabulated as positive, that is, as containing a gastric secretory depressant, unless at least three positive experiments, using at least two different animals, were obtained. In regard to the controls, the criteria were not as strict, since if two positive experiments were obtained, the extract was regarded as containing a gastric secretory depressant.

Experiment A.—Summarized in Table I: Of 22 achlorhydric carcinomatous stomachs, 11, or 50 per cent of the series, contained the secretory depressant; 156 individual experiments were performed.

TABLE I

SUMMARY OF RESULTS OBTAINED WITH BOILING WATER OR 0.2 PER CENT HCL EXTRACTS OF 22 ACHLORHYDRIC CARCINOMATOUS STOMACHS

Patient	No. of Exper's. Performed	Results
1. Boh	3	3 ++++
2. Liss*	8	3 ++++; 3 +++; 2 −
3. Gur	5	5 −
4. Young	6	4 ++++; 1 ++; 1 −
5. Litwin	6	2 ++++; 1 +++; 3 −
6. Behn	7	1 ++++; 2 +; 4 −
7. Brash	6	6 −
8. Reid	9	9 −
9. Benhn	7	7 −
10. Kruse	6	6 −
11. Holsw	8	8 −
12. Marc	9	3 ++; 6 −
13. Herbd	7	7 −
14. Weav	8	3 +; 5 −
15. Saks	14	2 +++; 1 ++; 3 +; 8 −
16. Han†	2	1 ++; 1 +
17. Boul	11	1 ++++; 1 ++; 3 +; 6 −
18. Edmund	10	1 +++; 1 + +; 1 +; 7 −
19. Bick	2	2 −
20. Loz.‡	7	1 +++; 1 +; 4 −
21. Lars‡	9	2 +; 7 −
22. Groeg	5	5 −

* Maximum free acid with histamine = 20; considered as definitely hypochlorhydric and, therefore, included in this group as a stomach whose secretions were inhibited as compared with the average normal.

† The small number of experiments performed here was due to the fact that the extract was obtained from a metastatic lymph node removed at operation from a patient with extensive inoperable carcinoma of the stomach.

‡ These extracts are considered as negative for the gastric secretory depressant since only two and not at least three positive experiments were obtained in the series run with them.

Experiment B.—Summarized in Table II: Of 12 carcinomatous stomachs secreting free acid, three, or 25 per cent, contained the secretory depressant; 80 individual experiments were performed.

Experiment C.—Summarized in Table III: A variety of control extracts were employed including those of stomachs from patients not exhibiting tumors or with tumors outside the stomach, and of a variety of neoplasms themselves. A total of 528 individual experiments were performed with a positive incidence varying from zero to 24 per cent, depending upon the group in question.

TABLE II

SUMMARY OF RESULTS OBTAINED WITH EXTRACTS OF CARCINOMATOUS STOMACHS WHICH CLINICALLY SECRETED NORMAL CONCENTRATIONS OF FREE HCL

Patient	Max. Free HCl (Histamine)	No. of Exper's. Performed	Results
1. Horwath	25 (Ewald test only)	6	3 ++++; 3 −
2. Yavitz	60	4	4 −
3. Sezeb	35	7	7 −
4. Sckm	55	6	6 −
5. Lev	40	9	1 ++++; 1 +++; 1 ++; 6 −
6. Kid	50	5	5 −
7. Urik	72	7	7 −
8. Pusat	30	8	8 −
9. Pop	50	3	3 −
10. Pal	110	7	7 −
11. Levins	110	8	3 ++++; 5 −
12. Schaub	82	5	5 −

TABLE III

SUMMARY OF INCIDENCE OF EXTRACTS CONTAINING GASTRIC SECRETORY DEPRESSANT

Extract	No. of Samples Tested	Per Cent with Gastric Secretory Depressant
Achlorhydric carcinomatous stomachs	22	50%
Carcinomatous stomachs secreting normal concentrations of free HCl	12	25%
Stomachs from patients not presenting malignant neoplasms	39	16%
Stomachs from patients with malignant neoplasms outside the stomach	34	24%
Carcinomata of the colon	17	12%
Colon mucosa adjacent to carcinoma of colon	11	0%

Prolongation of Achlorhydria by Repeated Injections of Gastric Secretory Depressant.—In order to rule out the possibility that the transitory hyposecretion and achlorhydria observed in some of the above observations was of the nature of a "shock reaction," and independent, to a large extent, of the quantity of extract injected, experiments were conducted in which positive extracts from achlorhydric carcinomatous stomachs were injected at frequent intervals, and in this manner the achlorhydria was prolonged, in one case for eight hours, depending upon the number of such injections. Repeated injections of positive control extracts also resulted in more prolonged hyposecretion and achlorhydria than when only one injection of the extract was made.

Discussion.—A number of factors that might have afforded inhibition of pouch secretion, other than some secretory depressant in the extracts, were considered and by experiment ruled out, such as prolonged depression of blood pressure, enterogastron produced in the usual manner,[6, 7] reduction in CO_2 combining power of the blood, high dextrose content in the extracts, usual bacterial toxins, temperature elevations in the test animals, *etc.* While some extracts, on occasion, produced severe depression or episodes of vomiting, these were by no means characteristic of the extracts from carcinomatous stomachs but were observed with control extracts as well. Depression and vomiting alone were not sufficient to cause positive results.

The incidence of positive control experiments is too large to be dismissed simply as "false positives." Furthermore, a review of the literature and our experiences have shown that a wide variety of unrelated substances such as urine, concentrated glucose solutions, extracts of various normal tissues, *etc.*, will, on occasion, when injected into pouch-dogs, produce transitory inhibition of gastric secretion and liberation of free acid. Atropine regularly produces such an effect. Thus, in an evaluation of the data obtained in the above experiments, it is necessary to bear in mind that an appreciable incidence of "nonspecific" positive experiments are obtained in a study of this kind.

The incidence of positive extracts from carcinomatous stomachs, which secreted normal or high acid gastric juice, closely approximates the incidence found among control stomachs from patients without neoplasms anywhere in the body. This, of course, is what might be predicted if the premise is accepted that achlorhydria accompanying gastric cancer is due to a local excess of a gastric secretory inhibitor; for if a stomach continues to secrete normal or high concentrations of free HCl although developing a cancer, a series of such stomachs should (and did) yield results practically identical with a series of experiments performed with stomach extracts from patients not presenting neoplasms anywhere in the body.

CONCLUSIONS

Boiling water or 0.2 per cent HCl extracts of the mucosae and neoplasms or achlorhydric carcinomatous stomachs, when neutralized and injected intravenously in dogs with stimulated gastric pouches, resulted in a marked depression of pouch section and achlorhydria with 11 or 50 per cent of 22 extracts studied. Similar depressant effects were noted with 14 or 19 per cent of 73 extracts of stomachs not presenting benign or malignant neoplasms.

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SURGICAL EMERGENCIES DURING CHILDHOOD CAUSED BY MECKEL'S DIVERTICULUM

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THE CONTRIBUTIONS to medical science distinguished by the name of Meckel were not all made by one man, as we are apt to assume, but by four men closely related to one another. Johann Frederick Meckel, the younger (1781–1833), belonged to the third generation of this remarkable family of anatomists. Among his contemporaries he was chiefly esteemed for a scholarly translation, from the Latin, of Wolff's monograph on the development of the intestines. To-day, we remember best his study of the pouch-like structure which not infrequently projects from the small intestine at a distance above the ileocecal valve, varying from 3 to 100 cm.

Meckel's diverticulum represents a remnant of the omphalomesenteric duct through which nourishment passes from the yolk sac to the embryo, in oviparous animals, like the chick.* In viviparous animals, such a need does not exist; and though present in the earliest stages of human development, the duct has no function to perform. Generally, the structure has vanished by the time of the child's birth, but not always. Whenever persistent, it becomes a menace to health.

Not only this intestinal pouch, but still other remnants of the omphalomesenteric duct occasionally plague their possessors. Malformations of that origin have been thought sufficiently important for classification as follows: (1) Pervious fistula running the full length of the duct. (2) Umbilical sinus. (3) Umbilical cyst. (4) Enterocystoma. (5) Fibrous cord attaching the umbilicus to the ileum. (6) Meckel's diverticulum.

The defect most often encountered is the diverticulum. At autopsy its incidence is roundly 2 per cent; and, oddly enough, it persists more often in the male sex. Thus, of the 19 patients in this report, 17 were boys and two were girls.

R. H. Fitz,[2] the pioneer American investigator of the clinical manifestations attributed to the vermiform appendix, took a deep interest in the comparable intestinal complications caused by Meckel's diverticulum. In the mature opinion of Fitz: "We owe to Meckel not only the almost universal acceptance of his theory of origin of the pouch in question, but also are indebted to him for calling conspicuous attention to its importance in the causation of serious disease."

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* An admirable account of the embryology of the umbilical region will be found in Prof. Max Brodel's Chapter 1 of Cullen's Monograph on "The Umbilicus." Saunders, Philadelphia and London. 1916.

TABLE I

SYNOPSIS OF THE CLINICAL AND PATHOLOGIC DATA IN 19 CASES WITH MECKEL'S DIVERTICULA

Case	Sex	Age	Abd. Pain	Emesis	Melena	Hb. (Sahli)	W.B.C.	Duration of Symptoms	Postoperative Diagnosis	End-result
1	M.	8 yrs.	Yes	Yes	Yes	25%	6,700	7 days	Giant diverticulum; with perforating ulcer of ileum.	Recovery
2	M.	11 mos.	Yes	Yes	0	51%	25,350	14 hours	Diverticulum; with intra-abdominal hemorrhage.	Recovery
3	M.	2½ yrs.	Yes	Yes	Yes	52%	11,450	1 year	Diverticulum; with bleeding peptic ulcer of ileum.	Recovery
4	M.	6½ yrs.	Yes	0	Yes	36%	11,000	2 weeks	Diverticulum; with bleeding peptic ulcer of ileum.	Recovery
5	M.	6 mos.	0	0	Yes	32%	9,350	Intermittent 1 month	Diverticulum; with hemorrhage.	Death
6	M.	1 yr.	0	0	Yes	42%	14,200	Intermittent since age 3 months	Diverticulum; with hemorrhage.	Death
7	M.	7 wks.	?	Yes	0	56%	7,550	4 days	Acute intestinal obstruction caused by fibrous diverticulum.	Recovery
8	M.	5 yrs.	Yes	Yes	0	75%	15,300	24 hours	Acute intestinal obstruction caused by bands.	Recovery
9	M.	19 mos.	Yes	Yes	Yes	Not taken		30 hours	Acute intestinal obstruction caused by adhesions.	Death
10	M.	3 yrs.	Yes	Yes	0	82%	13,950	24 hours	Diverticulum causing acute intestinal obstruction.	Recovery
11	M.	5½ mos.	Yes	Yes	Yes	75%	16,950	10 hours	Diverticulum; with acute intussusception.	Recovery
12	F.	7 yrs.	Yes	Yes	0	75%	16,900	48 hours	Diverticulum; with acute intussusception.	Death
13	M.	11 mos.	Yes	Yes	Yes	71%	8,550	5 days	Diverticulum; with acute intussusception.	Recovery
14	F.	3 mos.	?	Yes	0	47%	22,000	48 hours	Volvulus.	Death
15	M.	17 hrs.	Abdominal distention			Not taken		Since birth	Prenatal gangrene of diverticulum; with peritonitis.	Death
16	M.	5½ yrs.	Yes	Yes	0	70%	16,600	20 hours	Diverticulitis; with perforation.	Recovery
17	M.	2½ yrs.	Yes	Yes	0	80%	6,000	4 days	Diverticulitis; with perforation.	Death
18	M.	11 mos.	0	0	0	46%	8,150	Since birth	Diverticulum; with umbilical fistula.	Recovery
19	M.	4 wks.	0	0	0	105%	12,500	Since birth	Diverticulum; with umbilical fecal fistula.	Recovery

Pathologic Anatomy.—The resection of a gigantic specimen, described in the first of the appended case reports, excited my interest in Meckel's diverticulum. Consequently, pertinent cases of my own, as well as those operated upon by my colleagues at the Children's Hospital, were collected. Together, they formed a series worthy of analysis.

The specimen just mentioned (Case 1), which measured 38½ inches in length, was longer than any of which we have found record. Moll[3] described

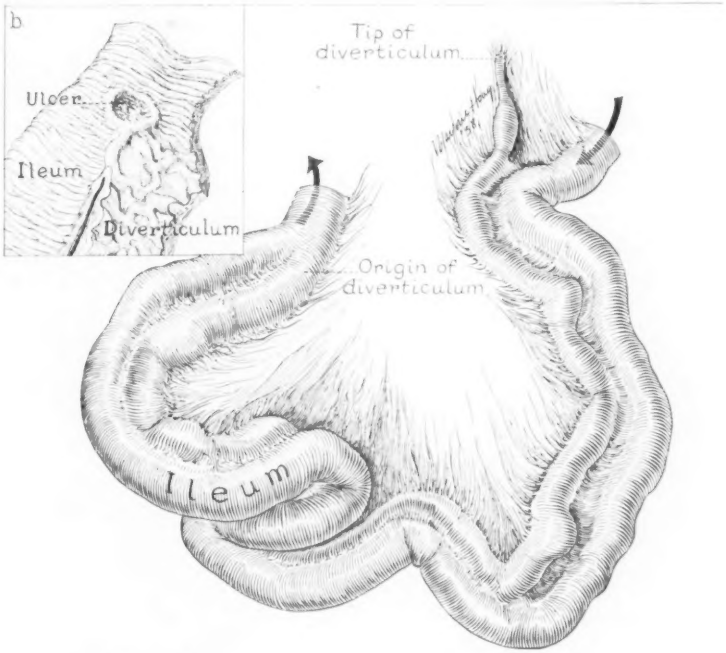

FIG. 1.—Case 1: Drawing of the giant diverticulum (duplex ileum) as it appeared at operation. It measured 38½ inches in length and was resected together with 37 inches of the adjacent ileum. Inset (b) shows the point of origin of the diverticulum and the large rugae of its mucosa, resembling, identically, those of the stomach mucosa, also the large perforating ulcer at the distal end of the resected ileum.

a diverticulum 33½ inches long in an infant five months old. Previously, Pollard[4] had reported a newborn with a diverticulum of 36 inches long that began 24 inches below the pylorus and ended as a huge culdesac in the umbilical cord. The term "duplex ileum" is applicable to a large intramesenteric diverticulum, such as the specimen of Moll, Pollard, and the one shown in Figures 1 and 1A.

True diverticula represent a continuation of the intestine, and their walls contain the same histologic structures as those of the intestine. *False diverticula*, on the contrary, do not possess a muscular coat. Utilizing this criterion, it has been established that intramesenteric diverticula belong to the true variety; yet, it is difficult to explain their peculiar location. Theories, to be sure, have been advanced to account for the transposition of the pouch; and,

because it is the most satisfactory, the hypothesis of Moll should be quoted. Initially in the embryo, he argues, the diverticulum always springs from the antimesenteric side of the intestine, and has a mesodiverticulum through which runs the vitelline (omphalomesenteric) artery. As involution proceeds to obliterate this blood vessel, it becomes shorter and shorter. Sometimes, Moll believes, the resultant traction draws the diverticulum upwards toward the border of the mesentery, tangential to the bowel. Then adhesions form, the previous vascular supply disappears, and a new one develops from arteries in the intestine. Furthermore, Moll assumes that long diverticula are caused by the premature withdrawal of the bowel away from the umbilical region, toward the peritoneal cavity.

The mucosa in the specimen in Case 1 was identical with gastric mucous

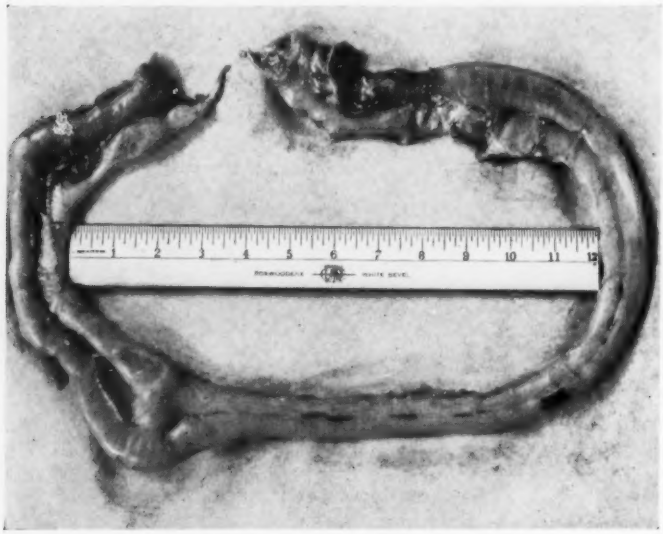

FIG. 1 A.—Case 1: Photograph of the gross specimen of the resected diverticulum and the adjacent ileum.

membrane. In keeping with the observations of Curd[5] and others, the ulceration in this instance did not lie within the heterotopic gastric tissue, but in the adjacent ileum opposite the mouth of the diverticulum. Everyone agrees that lesions of this type are caused by the hydrochloric acid and pepsin which the heterotopic mucosa secretes. Ulceration, however, has been observed in diverticula where no trace of gastric mucosal histology was demonstrable.

No matter what their causation, ulcers may bleed, perforate, and initiate a peritonitis. Of exceptional interest is the case reported by Greenblatt, Pund and Chaney[6] in which a tumor of the diverticulum was mistaken for a duodenal ulcer, and after its removal the diverticulum was found to contain gastric mucosa, Brunner's glands, pancreatic tissue and a structure resembling a biliary duct. Other types of tumors, too, have been traced to the diverticulum;

Mathews[8] reported a malignant leiomyoma, Kadinsky, a "carcinoid" tumor, and Wisely, a medullary carcinoma.

The relative frequency of the familiar complications caused by Meckel's diverticulum is illustrated in the study of 201 cases by Miller and Wallace[7]: (1) Ulcers with hemorrhage, perforation, or both, occurred in 93 cases. (2) Intussusception in 63. (3) Other types of ileus in 26. (4) Acute inflammation in ten. (5) Miscellaneous complications in nine.

Our own, much smaller, series includes representatives of all these groups. Hemorrhage, which is always conspicuous in analytic reports of this kind,

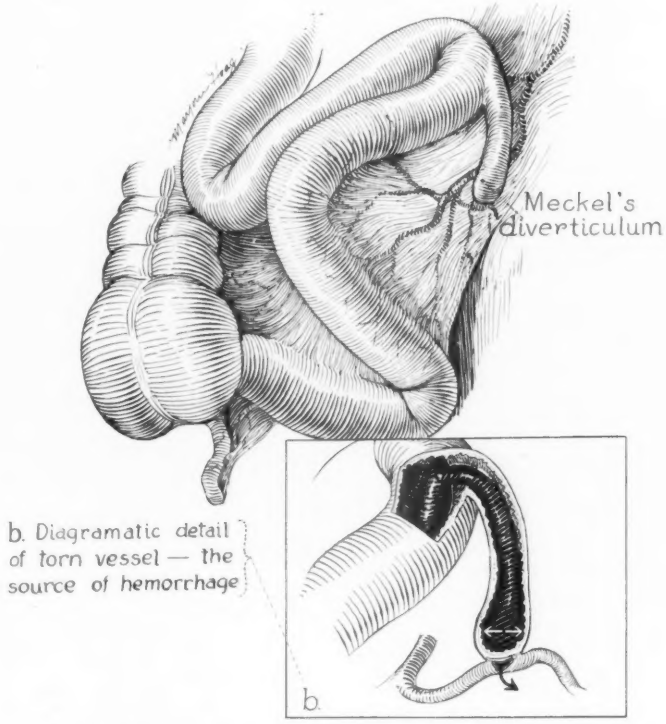

FIG. 2.—Case 2: Drawing showing a Meckel's diverticulum, the distal end of which had become adherent to the undersurface of the mesentery. Inset (b) shows, diagrammatically, the gross pathology at the site of its detachment, which resulted in the tearing of a blood vessel and consequent intra-abdominal hemorrhage.

had an unusual, if not unique, causation in Case 2. There, upon opening the abdomen, free blood escaped, and the terminal ileum was apparently full of blood. As the operation progressed, the distal end of the diverticulum was found located beneath the mesentery, pulled into a pocket where it had been fastened by adhesions. For some reason, unidentified, the adhesions had broken loose at one point, and a small mesenteric vessel had been torn across. A ligation of the vessel controlled the hemorrhage completely.

Harkins[9] estimated that intussusception accounted for 17 per cent of the complications attributable to Meckel's diverticulum. The complex character

of the mechanism at times is illustrated by Cases 11, 12 and 13. In Case 11, one foot of small intestine had telescoped into the ileum, and this, in turn, had passed through the ileocecal valve. The ascending colon also had telescoped into the transverse colon as far as the splenic flexure.

When a remnant of the omphalomesenteric duct provokes vovulus in a child, the prognosis is less favorable than with this type of ileus in an adult. A profound circulatory disturbance quickly leads to gangrene and peritonitis. The outlook is particularly serious if the twist has been initiated by a cord attaching the ileum to the umbilicus, to a viscus or to the mesentery. Death was the result of such a mechanism in Case 14.

FIG. 3.—Case 5: Roentgenogram showing the presence of a Meckel's diverticulum.

Of course, bands may cause obstruction other than volvulus. Thus in Cases 7 and 8, a segment of ileum had become obstructed at two different levels as it looped under a fibrous cord derived from a Meckel's diverticulum. In Case 7, the cord was attached to the convex surface of the ileum just above the higher level of obstruction, and passed over the intestine a second time near the ileocecal valve. Shortly after the band was cut, the intestine resumed its normal color.

Prenatal complications are exemplified in Case 15, where death, 17 hours after birth, was due to gangrene of the diverticulum. Boikan,[10] in making report of a similar situation, which he called "meconium peritonitis," has reviewed the literature on this subject.

The umbilical fistulae of Cases 18 and 19 are examples of one of the most interesting, but least common, complications. Embryologists have not been able to explain satisfactorily the rare finding, in Case 18, of gastric mucous membrane lining the umbilical end of the pouch and small intestine mucous membrane lining the ilial end (Fig. 5).

Other congenital defects, associated with cases in this series, were pyloric stenosis (Case 9), for which an operation had been previously performed; and mongolianism (Case 17). Christie[11] noted additional abnormalities in more than 30 per cent of his 63 cases of persistent diverticula.

COMMENT.—The vast majority of diverticula lie free in the peritoneal cavity and, therefore, give no inconvenience. Although a blind pouch, it seldom

entraps foreign bodies; through its wide mouth they have an easy exit into the lumen of the bowel. In this respect the diverticulum differs from the appendix but, like the appendix, it frequently becomes the seat of an inflammatory process; and the resulting symptoms are so much alike, in both instances, that they may rarely be distinguished. In Case 6 chronic diverticulitis was mistaken for appendicitis.

Nearly always, the prevalent symptoms arise from one of the various complications to which the diverticulum is subject. Thus, it has been found among the contents of a hernial sac—inguinal, femoral or umbilical. Symptoms at other times are referable to the ulceration; bleeding and perforation have already been discussed. Likewise, in the section on pathologic anatomy, the intimate relationship between the diverticulum and intestinal obstruction was

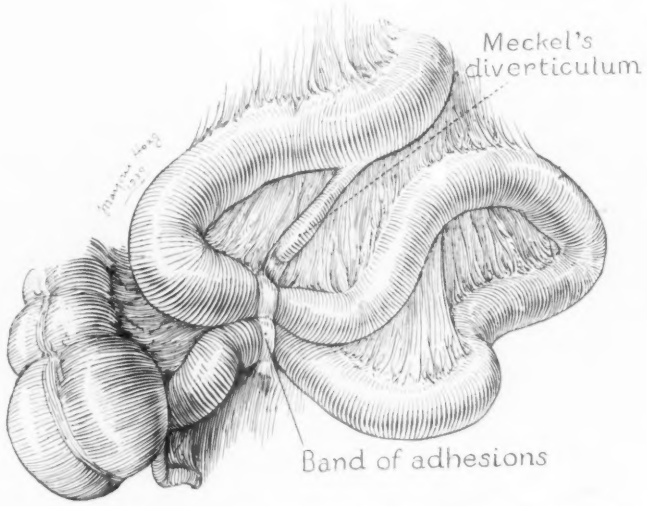

FIG. 4.—Case 7: Drawing showing the operative pathology in this instance of Meckel's diverticulum, the fibrous tip of which had become attached to the root of the mesentery resulting in the obstruction of the terminal ileum at two levels.

considered, and it follows that frequently symptoms of ileus alone are present when, in reality, a persistent diverticulum is the root of the trouble.

So variable, indeed, are the complications in question, that, whenever the surgeon is called upon to treat an abdominal emergency, especially during childhood, the preliminary diagnosis should take into account a persistent diverticulum as the basic factor in the problem; and, at the time of operation, exploration should always establish the presence or absence of this structure.

The clinical manifestations, never specific, merely point to a severe disturbance somewhere within the abdomen, which becomes distended and exhibits muscular rigidity either locally or generally. Most significant among the subjective symptoms are pain, nausea and vomiting, sometimes constipation, more often small evacuations containing blood. The laboratory findings may indicate an anemia (hemoglobin in this series varied from 25 to 105 per

cent) or an infection (leukocytes varied from 6,000 to 25,000); but, on the whole, the blood picture proves to be helpful in diagnosis only when integrated with the facts gathered from the history and physical examination of the patient. Radiography has a very limited usefulness. In Case 5, to be sure,

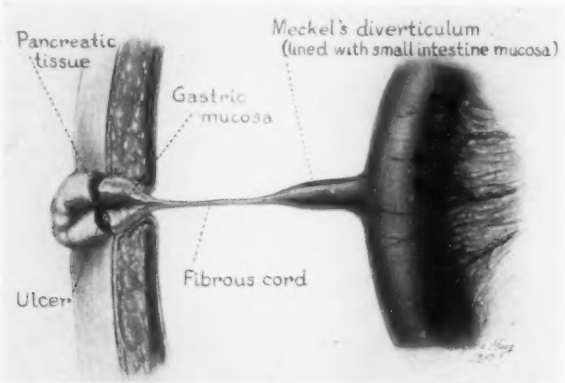

FIG. 5.—Case 18: Drawing showing the operative pathology of an umbilical sinus which connected with a Meckel's diverticulum.

the correct diagnosis was made by the roentgenologist, yet this experience suggested nothing in the way of a principle capable of wide application.

The period of time elapsing between the onset of symptoms and the requisite surgical operation, varied from a few hours to several years in this series of cases. A review of the records demonstrates, as could be predicted, that the duration of the illness and the efficacy of surgery have a direct re-

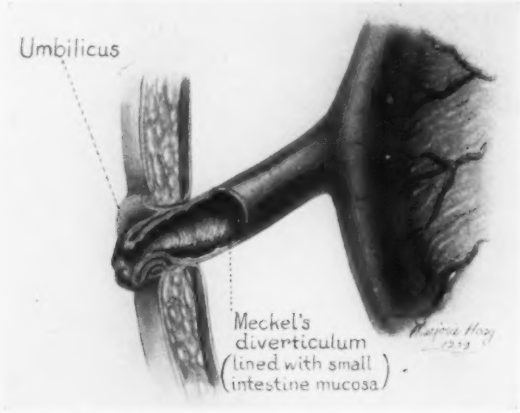

FIG. 6.—Case 19: Drawing showing the operative pathology in an instance of an umbilical fecal fistula which connected with a Meckel's diverticulum.

lationship. Early diagnosis promotes a smooth convalescence and recovery. But, technical factors also enter largely into the character of the results the surgeon obtains. Anyone who has merely seen a diverticulum of the usual

type at autopsy or a chance finding during a celiotomy will be impressed with its resemblance to the vermiform appendix; and he may assume that the removal of either structure should be equally simple. That conclusion, however, overlooks the fact that, usually, multiple pathology must be treated when a diverticulum becomes the indication for an operation.

And, besides, the technic of appendicectomy differs notably from that of removal of a diverticulum, even when the underlying pathology consists of nothing more than an acute inflammation. Hudson[12] has correctly emphasized the risks, especially in children, of inverting a diverticulum stump with a purse string suture. Too often, as in Case 6, edema and occlusion of the bowel cause death. To avert that result, the aperture in the intestinal wall after removal of a diverticulum should be closed in layers, transverse to the long axis of the bowel, just as after the intestine has been opened to remove a polyp or a foreign body.

Mortality.—Among the 19 cases in this series, there were seven deaths, a mortality of approximately 37 per cent. The youngest patient was a newborn infant, the oldest a child of eight years. The ages of these children increased the surgical hazards, especially since some of the operations were performed before present-day facilities became available to combat under-nourishment, hemorrhage, acidosis and dehydration.

SUMMARY AND CONCLUSIONS

The analysis of 19 celiotomies upon children, occasioned by persistent Meckel's diverticula, includes the description of a specimen, longer than any previously reported—a "duplex ileum." Other cases illustrate the familiar complications attributable to this vestigial structure—hemorrhage, ulceration, perforation, peritonitis, intussusception, volvulus, intestinal obstruction, umbilical sinus, and umbilical fecal fistula. Gangrene in one instance occurred during intra-uterine life, so-called "meconium peritonitis."

The surgeon should never overlook a diverticulum as the possible source of the trouble whenever he is called upon to treat an acute abdominal emergency during childhood. In abdominal section for acute intestinal obstruction, where symptoms do not call for exploration of a particular portion, the incision should be made in the right lower quadrant. The region of the umbilicus and the terminal three feet of the ileum should receive first attention. If a band is found, it is most likely the remains of a persistent vitelline duct or an omphalomesenteric vessel. The pediatrician must also bear this diagnosis in mind when faced with cases of indefinite abdominal pain accompanied by periodic mild anemia and low grade, unexplained fever.

The postoperative result was recovery in 12, and death in seven cases. Inversion of the stump with a purse string suture, responsible for one fatality, is a hazardous procedure in children, because subsequent edema may completely block the lumen of the intestine. Only by early operation, can a satisfactory mortality rate be obtained.

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ACUTE THROMBOCYTOPENIC PURPURA HEMORRHAGICA ASSOCIATED WITH TUBERCULOSIS (MILIARY) OF THE SPLEEN

SPLENECTOMY—RECOVERY

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WINTERNITZ,[1] in 1912, advanced the opinion that primary tuberculosis of the spleen may not mean that the spleen is the portal of entry of the organism, or the first tissue of the body in which the disease manifests itself, but that the tuberculous process may localize itself in the spleen which acts as a focus for dissemination of the tubercle bacilli, and that the original focus may remain entirely quiescent. In a careful analysis of 51 cases of tuberculosis of the spleen, he found two instances in which the skin showed evidences of purpura or ecchymosis.

The case of miliary tuberculosis of the spleen, herewith reported, showed no tuberculous lesions arrested or active in any other part of the body, and would very appropriately be placed in the classification of Winternitz's primary tuberculosis of the spleen. Another salient feature in this case was the fulminating character of the blood platelet disappearance, and their rapid reappearance following splenectomy. In view of the fact that the spleen was the only organ showing manifestations of miliary tuberculosis, the casual relation that miliary tuberculosis of the spleen appears to bear to acute thrombopenic purpura hemorrhagica is demonstrated by this case.

Purpuric diatheses, in association with tuberculosis, has been described in adults, and many pathologists have felt that the purpura was secondary to a toxemia. Bauch,[2] in 1916, reported three instances of purpura in adults with pulmonary tuberculosis, and his opinion was that the tubercle bacilli, or their toxins, acted as irritants to the endothelium of the cutaneous vessels and produced the hemorrhagic or purpuric spots. Another theory that Bauch has advanced is that the blood vessels may have undergone hyaline or amyloid changes with the resultant purpuric manifestations. Garin,[3] in 1920, in reviewing 26 cases, felt that the hemorrhagic purpura was secondary to the tuberculosis. Pratsicas,[4] in 1924, reported four cases, all of whom were found to have enlarged spleens, and in each instance exhibited purpuric manifestations—all cases came to autopsy. The ages given in three of the cases were 22, 22 and 23, respectively. Pratsicas believed that in two cases the cutaneous hemorrhages were embolic and in the third case the result of disseminated miliary tuberculosis. Villa,[5] in 1928, reported a singular observation in a female,

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age 38, who, after being confined to the hospital for two weeks, began to bleed from the gums, developed epistaxis, hematuria and melena, purpura on the body, and had an enlarged spleen and a reduced platelet count. The patient died five days after the purpuric manifestations appeared. Autopsy revealed evidences of miliary tuberculosis. Winternitz specifically states that all cases of tuberculosis of the spleen not operated upon died. Fifty-nine per cent of the cases who had splenectomies performed, survived. Kellert,[6] in 1931, reports a case of miliary tuberculosis of the spleen associated with thrombopenic purpura, in which instance the spleen was removed and the patient recovered. This was similar to the case herewith reported, except for the lesion of the lung. Andrus and Holman,[7] in 1939, reported 12 cases of thrombocytopenic purpura that recovered from the blood disorder following splenectomy. The case herewith reported, of miliary tuberculosis of the spleen with a fulminating thrombocytopenic purpura, also made a complete recovery following splenectomy.

Case Report.—Hosp. No. V-6709: C. B., male, age 42, was admitted to the Gouverneur Hospital, April 28, 1938, complaining of epistaxis and ecchymosis of the skin, of three days' duration. His mother died from hypertension, otherwise the family history was irrelevant. He had had the usual childhood diseases. He had been operated upon for glaucoma, at the age of nine; and had had an hemorrhoidectomy performed nine years ago. Negative venereal history.

The patient had been perfectly well until April 19, 1938 (three days prior to admission), when he noticed large blotches on his right arm. He was suddenly awakened the same night by what the patient described as "a sensation of feeling bloody pimples

LABORATORY DATA

	Preoperative		Postoperative			
	4/22/38	4/24	4/27	4/28	5/3	5/15
W.B.C.	10,000	6,700				9,800
Polys.	64	63%				68%
Lymph.	36	26%				32%
Monocytes	0	8%				
Eosin.	0	3%				
Platelets	40,000	5,000	200,000	300,000	500,000	500,000
R.B.C.	5,200,000	5,420,000	4,400,000		3,900,000	4,000,000
Hb.	126%	100%	82%		78%	85%
Bleeding time	10 min.	10 min.	2 min.			
Coagulation time	2½ min.					

4/22

Pinch and tourniquet tests were positive.

Fragility test: Maximum resistance 0.44%
Minimum resistance 0.32%

4/25

Blood sugar 101 mg.
N.P.N. 34 mg.
Wassermann negative

Urine Examinations

4/22	Benzidine	4 plus
	Albumin	2 plus
4/25	Benzidine	4 plus
	Albumin	2 plus
4/29	Benzidine	1 plus
	Albumin	trace
5/5	Benzidine	negative
	Albumin	negative

on his lips and mouth." The following morning he had a nose bleed, and black and blue as well as red spots appeared over his entire body. His condition became rapidly worse, and he complained of a tight sensation (pressure) over his entire head, and weakness. Just before admission to the hospital, he noticed that his urine was bloody.

Physical Examination.—Patient is acutely ill; hemic component good. Eyes: Right, cataract; left, previous glaucoma operation. Nose: Bloody crusts in right nasal passage. Mouth: Small ecchymotic spots present on lips, soft and hard palate and tongue. Neck: No adenopathy noted. Heart and lungs: Negative. Abdomen: Soft. No tumor mass palpable. Liver and spleen not enlarged. Neurologic status: Normal. Rectal examination: Negative. Skin: Large, painless ecchymotic areas over upper extremities and on right great toe. Smaller areas present over entire body—more purpuric than ecchymotic. Blood pressure preoperatively was 115–120/80. Postoperatively 118–132/80. Roentgenologic examination of the chest was negative for tuberculosis. *Diagnosis:* Acute thrombocytopenic purpura hemorrhagica.

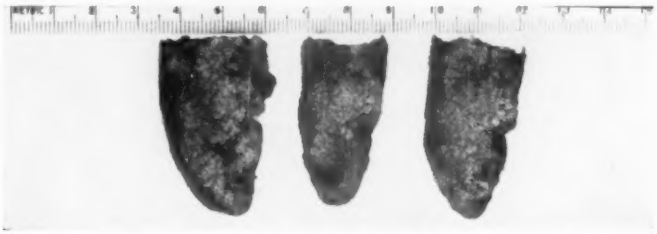

FIG. 1.—*Gross Pathology of Spleen:* The viscus measured 14x9x4 cm. and weighed 237 grams. The surface was smooth except in one area where there was a fibrous thickening about 1 cm. wide. The hilus appears normal. On section, the spleen cuts with resistance, and throughout there appears to be marked hyperplasia of the lymphatic structures. Nodules varying in size from 1 Mm. to 1 cm. are seen, many are confluent. No necrotic or caseous areas were found. The capsule appeared to be normal.

Recommendation.—(1) Conservative and expectant—which may lead to a remission of the acute stage. However, the danger in the method is the possibility of a cerebral hemorrhage or hemorrhage into some other vital organ. (2) Splenectomy—which is curative in majority of the cases, which latter was elected.

Operation.—April 26, 1938. Dr. Rupert F. Carter: Routine splenectomy. Convalescence was normal. Patient received 400 cc. of blood on the day of the operation, 300 cc. on April 27, 1938, and 350 cc. April 29, 1938.

Pathologic Examination.—Gross: Path. No. 4114. Drs. M. Kopel and D. Symmers: The spleen measured 14x9x4 cm. and weighed 237 grams. The surface was smooth except in one area where there was a fibrous thickening about 1 cm. wide. The hilus appeared normal. On section, the spleen cut with resistance, and throughout there appeared to be marked hyperplasia of the lymphatic structures. Nodules varying in size from 1 Mm. to 1 cm. were noted, many confluent. No necrotic or caseous areas were found. The capsule appeared to be normal (Fig. 1).

Microscopically, the capsule and trabeculae appeared thickened and fibrous; pulp congested with red cells; sinuses dilated; malpighian corpuscles hyperplastic; central arteries of the malpighian corpuscles thickened (Fig. 2). *Pathologic Diagnosis:* Miliary tuberculosis of the spleen.

Follow-Up Record.—Readmitted, April 11, 1939, for check-up examination. The patient had gained weight; general condition good; no complaint; feels well. A roentgenogram of the chest showed the heart slightly enlarged to the left. Slight accentuation of the aorta. Hilus markings increased. Lungs: Increased pulmonic markings throughout. Interlobar pleura is visualized. Diaphragm normal. Costophrenic spaces

clear. *Follow-Up Conclusions:* Slightly enlarged heart. Secondary congestive lung changes.

Laboratory Data.—Amount of urine in 24 hours—1,100 cc. Vitamin C in 24-hour urine—34.1 mg. Vitamin C in 100 cc. of urine—3.1 mg. Stool—negative. Sputum—negative for tubercle bacilli. Sediment rate—nine millimeters in one hour.

Blood Examination.—April 20, 1939: Hemoglobin 96 per cent; R.B.C. 5,070,000; W.B.C. 9,400; nonsegmented polys. 5; segmented polys. 28; eosinophiles 3; basophiles 1; lymphocytes 52; monocytes 12; platelets 320,000.

The platelet count is normal. Relative lymphocytosis and mononucleosis is what one would expect to find in a patient who has had a splenectomy for miliary tuberculosis.

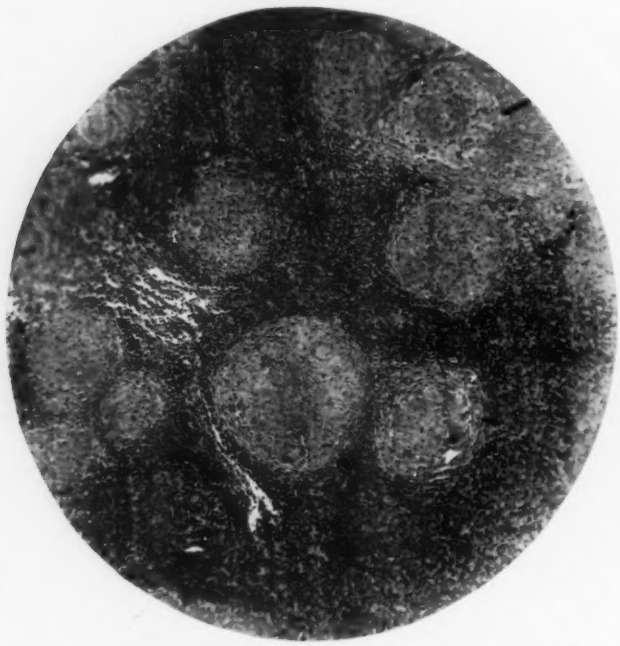

FIG. 2.—Photomicrograph showing, scattered throughout the spleen, numerous centrally pink-stained tubercles, surrounded by epithelioid cells accompanied by Langhan's giant cells. Some of these are surrounded by a wall of lymphocytes, others by a thin fibrous tissue capsule. Diagnosis: Miliary tuberculosis of the spleen.

Montoux test: Right forearm (1/1,000)—24 hours—1 plus; 48 hours—1 plus. Bleeding time—3 min., 10 sec. Coagulation time—4 min., 20 sec.

Fragility test (Rumpel-Leed): Four petechial areas in area three inches below tourniquet (normal manifestation). R.B.C. fragility hemolysis begins at 0.40 per cent and ends at 0.28 per cent—indicating decreased fragility (normal fragility 0.34 to 0.44).

SUMMARY

(1) A case of tuberculosis of the spleen (with miliary tubercles) associated with acute thrombopenic purpura is presented.

(2) Splenectomy was followed by complete recovery.

(3) A check-up blood examination, one year later, revealed a normal platelet count and a relative lymphocytosis.

(4) The general condition of the patient is good, and he has gained 40 pounds during the past year.

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THE USE OF ERGOTOXINE AND ERGOTAMINE IN THE SURGICAL MANAGEMENT OF THYROTOXICOSIS*

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ELLIOT,[1] in 1904, postulated that adrenalin mimicked the action of the sympathetic nerves, and even suggested that adrenalin might act as the intermediate agent between nerve ending and the organ. This conception later received much support and was greatly enlarged by the contributions of Loewi,[2,3] Dale,[4,5,6,7] and many others.

In 1906, Dale[8] first showed the capacity for ergot preparations to abolish this sympathetic effect. In other words, ergot preparations have the quality of preventing the action of adrenalin. According to Barger,[9] the preparation used by Dale was chrysotoxin, which contained 2 per cent of ergotoxine, and this latter is undoubtedly the effective substance. The isolation of ergotoxine by Barger and Carr,[10] the same year, made possible a more precise and efficient application of this principle, and this was further supplemented by the discovery of ergotamine, in 1920, by Stoll.[11] Ergotoxine and ergotamine have similar pharmacologic actions (Clark[12]).

In 1927, Navratil[13] showed that stimulation of an accelerator nerve of an ergotaminized heart still results in the production of the accelerating substance, adrenalin, but it does not show the usual action upon the heart. This might be interpreted by considering that ergotamine occupies certain pattern-cell receptors, thereby preventing the adsorption of adrenalin on these same receptors so that no accelerating effect can take place.

The pharmacologic literature concerning the ergot alkaloids is unusually extensive and well known, but any clinical application finds rather uncertain support from the frequently confusing and sometimes conflicting contributions. The observations reported in this investigation bring definite clinical evidence regarding the ergotoxine-ergotamine-adrenalin relationship. One of the most distressing phenomena in the surgical management of thyrotoxicosis is the associated tachycardia. This fact is so well known among surgeons that any further discussion would be superfluous. However, a study of the operative and postoperative periods of patients subjected to thyroidectomy offers ample evidence to confirm this clinical experience. In an effort to minimize this cardiac reaction to surgery the following rationale was evolved which

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led to the use of ergotoxine and ergotamine in a series of cases of thyroidectomies for thyrotoxicosis.

In the surgical treatment of thyrotoxicosis there are two periods during which tachycardia becomes a most serious and alarming manifestation: (1) During operation. (2) Twenty-four to 72 hours postoperatively—the period of so-called crises.

The tachycardia occurring during operation is not susceptible of explanation on the basis of thyroxin activity alone, because thyroxin effects ought not to appear for at least 12 hours, and usually are evident only after 24 to 36 hours. This tachycardia, then, would seem best explained by an increased output of adrenalin as a result of the subjective sensations of anxiety, fear, *etc.*, and those objective considerations of trauma, blood loss, anoxia, *etc.* This excess would have the most pronounced effect upon the cardiac rate because thyroxin specifically potentiates the action of adrenalin on the specific tissue or the myocardium.

On the other hand, the tachycardia occurring during the crises might very properly be explained upon the basis of a thyroxin effect because of its operative release 24 to 72 hours previously, and the potentiation of a relatively normal adrenalin production. Therefore, in the operative reaction, adrenalin is a major factor and thyroxin a minor one, while in the crises, thyroxin is the major factor and adrenalin the minor one.

Accordingly, the operative tachycardia should be susceptible to more efficient control by ergotoxine and ergotamine than that of the postoperative period—this has been found to be the case. Incidentally, in the cases presented, ergotoxine and ergotamine had no effect on the anoxic tachycardia, and they illustrate rather clearly the high value, in fact, the necessity for a supplemental oxygen supply in postoperative cases of thyrotoxicosis. The last 15 consecutive cases of thyrotoxicosis observed form the basis of this report and the response obtained was interpreted as favorable in all instances. The details of five cases are herewith presented to illustrate the different reactions encountered during this investigation, and to exemplify the experiences with the cases thus far observed.

CASE REPORTS

Case 1.—Met. No. 966: L. D., white, female, age 56, was admitted to the Metropolitan Hospital, January 23, 1939, with a basal metabolic rate of plus 53, and a pulse rate of 118. Under iodine therapy and usual preoperative regimen the pulse rate gradually fell; on February, the basal metabolic rate was plus 40, on the seventh, plus 36, and on the ninth, plus 19.

Under cyclopropane anesthesia, operation was begun at 9:20 A.M., February 14. At 10:35 A.M. the pulse rate had risen to 120 and ¼ mg. ergotamine was administered. Operation was completed at 11:00 A.M., and the pulse rate had fallen to 96.

The next morning, at 9:00 A.M., the temperature was 106° F., and the pulse rate 110. The next afternoon, at 5:00 P.M., the temperature was 105.4° F., and the pulse rate 120. That evening, at 10:00 P.M., the temperature was 105.4° F., and the pulse rate 110. In view of these temperatures, the pulse rate remained relatively low (Chart 1). This pulse stability is probably related to three spaced doses of ergotamine during this time.

This case illustrates fair operative and good postoperative control of the pulse rate by ergotamine.

Case 2.—Hosp. No. 7681: A. O'L., white, female, age 48, was admitted to the Flower-Fifth Avenue Hospital, November 15, 1938, with a one-month history of illness. Exophthalmos was present; the basal metabolic rate before admission was plus 70 and the pulse rate 120. Under iodine therapy and usual preoperative regimen the pulse rate varied between 120 and 134 during the first week. On November 23, the basal

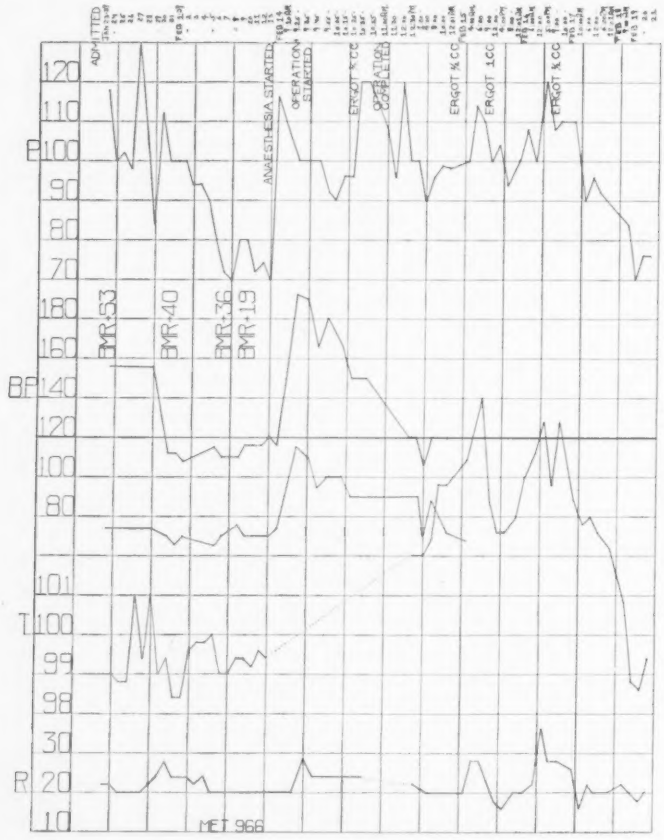

CHART 1.—Met. Hosp. No. 966: Shows rather good operative and postoperative control of pulse rate by ergotamine.

metabolic rate was plus 46. The pulse rate gradually became slower, to remain within the 90–100 division; on December 2, the basal metabolic rate was plus 21, on December 6, plus 20. The pulse rate was unstable most of the time.

On December 7, anesthesia with cyclopropane was begun at 2:18 P.M., when a high initial pulse rate appeared but which immediately came down on induction of anesthesia. At 2:42 P.M., the pulse rate had risen to 120, and ¼ mg. ergotamine was administered. In ten minutes the pulse rate was 108 and remained relatively well controlled and stabilized until operation was completed, at 3:45 P.M. At 3:55 P.M., the airway was removed and the pulse rose to 120 and remained in this vicinity for 48 hours.

This persistent high pulse level remained on an even plateau until the intro-

duction of intranasal oxygen, 48 hours later. This supplemental supply of oxygen resulted in a fall in pulse rate to 100 and then to 84, with a temporary rise when the oxygen was discontinued (Chart 2). The pulse rate during this 48-hour period was high but well stabilized, and the stability was attributed to four doses of ergotamine during this time, while the tachycardia would appear to be due to anoxia.

This patient illustrated singularly well the fact that ergotamine (or ergotoxine) had no effect on the tachycardia of anoxia, and that by this therapy

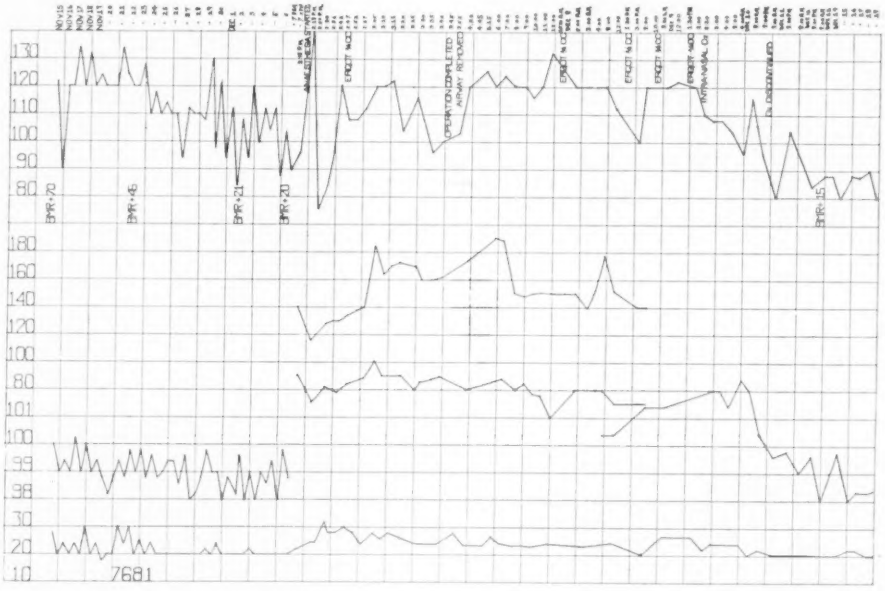

CHART 2.—Hosp. No. 7681: Shows marked pulse instability preoperatively, and relatively good postoperative stability after five doses of ergotamine. Also, on removal of the airway, pulse rate rose remaining to a relatively level plateau until the administration of intranasal oxygen, 48 hours later. This shows that an anoxic pulse is not effected by ergotamine.

the operative and postoperative pulse is more stable and better controlled than that of the preoperative period.

Case 3.—Hosp. No. 1514: B. T., white, female, age 40, was admitted to the Flower-Fifth Avenue Hospital, March 5, 1939, with a two-month history. There had been no exophthalmos but the basal metabolic rate was plus 60 on January 25, 1939. The symptoms entirely subsided under iodine therapy. She remained quite well for a few weeks but soon became worse. On March 7, the basal metabolic rate was plus 25, on March 15, plus 36.

Her pulse rate was unstable during this period and gradually increased in rate. Her condition did not improve with iodine therapy and operation was performed, April 1, 1939. The operation started at 10:18 A.M. (cyclopropane anesthesia), with an initial pulse rate of 90. At 10:55 A.M., the pulse rate had climbed to 154 when ½ mg. ergotamine was administered. Sixteen minutes later the pulse was 90. The pulse remained relatively well controlled, fluctuating between 105 and 130; at 12:44 P.M. the ergotamine was repeated. The operation was completed at 12:53 P.M., having required two hours, 35 minutes.

For some time the pulse rate did not exceed 120. Ergotamine (¼ mg.) was given

at 6:00 that evening and again at midnight. However, the next morning at 6:00 A.M. the pulse had risen to 160. Ergotamine was given again, but no definite effect was observed; at 7:30 A.M. the pulse rate had risen to 176 and the temperature to 105° F. Those in

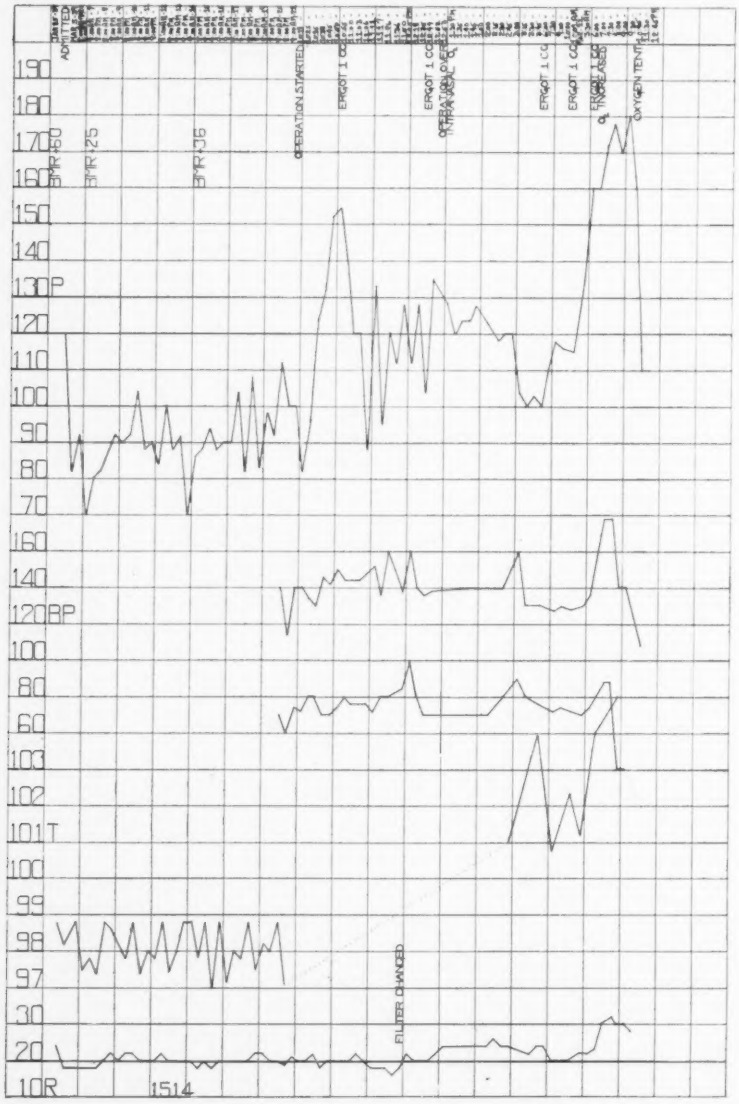

CHART 3.—Hosp. No. 1,514: Shows marked pulse instability before operation, with an increasing rate, a high operative peak, well controlled by ergotamine, and, in view of the severity of the reaction, a relatively good postoperative control. Near the end of the first 24 hours, anoxic symptoms developed and exitus took place, probably due to some respiratory accident.

attendance felt that this was undoubtedly, at least in part, a reaction to a mechanical anoxia; despite attempt at increasing oxygen supply, the patient expired about 1:00 P.M. (Chart 3).

Notwithstanding the unfortunate outcome of this case, ergotamine seems to have exerted a very definite control of the operative tachycardia and even the postoperative reaction until evidences of anoxia became very pronounced.

Case 4.—Met. No. 1189: M. D., white, female, age 62, was admitted to the Metropolitan Hospital, January 27, 1939. On February 6, the basal metabolic rate was plus 51. Under iodine therapy and the usual preoperative regimen the basal metabolic rate fell to plus 23 by February 20; during this intervening period the pulse rate fluctuated between 108 and 80.

Operation was begun at 9:00 A.M., February 21, and at 9:50 A.M., the pulse rate had risen to 126, so that ¼ mg. ergotamine was administered; at 10:00 A.M., the pulse was 90, remaining relatively well controlled until the operation was completed at 10:20 A.M.

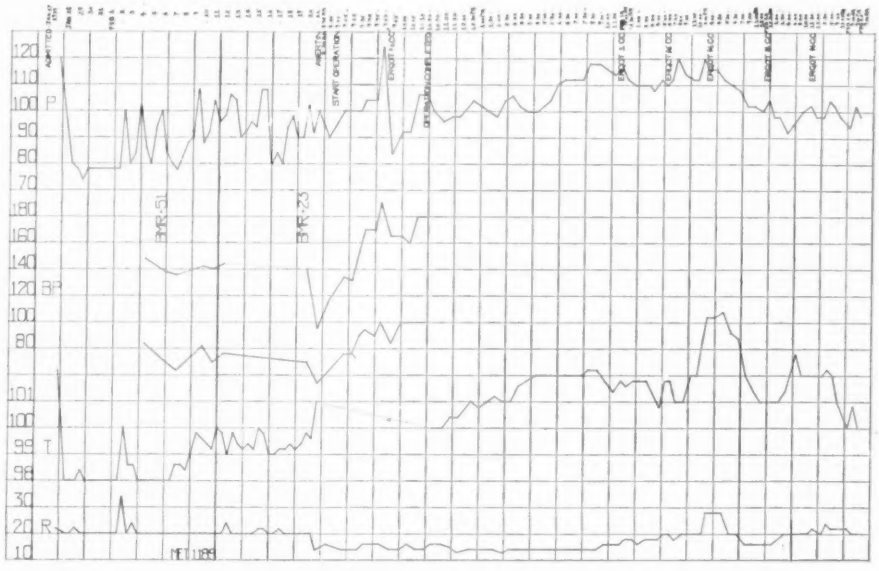

CHART 4.—Met. Hosp. No. 1,189: Shows control of the peak pulse rise during operation, and a relatively level postoperative plateau, after five doses of ergotamine. The pulse plateau, postoperatively, stands in marked contrast to its preoperative instability.

The patient received ½ mg. ergotamine five times during the course of the next 48 hours. This maintained the postoperative pulse rate on a relatively level plateau, which gradually fell to below 100 on the fourth postoperative day. In this instance, the temperature was 104.4° F., while the pulse rate remained under 120 (Chart 4).

This case shows good control of the peak pulse rise during operation and a relatively stable pulse rate postoperatively, which stands in marked contrast to its preoperative instability.

Case 5.—Met. No. 731: W. P., white, male, age 38, was admitted to the Metropolitan Hospital, January 18, 1939. The basal metabolic rate was plus 38 on January 20; on February 1, plus 35, and on February 9, plus 2. During this period the patient received iodine therapy and the usual preoperative regimen.

Operation, February 14, under cyclopropane, was begun at 11:35 A.M., when the pulse rate was 80. At 1:30 P.M., the pulse had risen to 156; ½ mg. ergotamine was ad-

ministered, and at 1:45 P.M., the pulse rate had fallen to 110, at which time operation was completed.

The pulse rate at midnight was 90, when ¼ mg. ergotamine was administered. The next morning it had risen to 118; after ½ mg. ergotamine was given, the pulse rate fell during early afternoon to below 100. The subsequent convalescence was uneventful (Chart 5).

This case illustrates a well-controlled peak operative rise with a rather stable pulse reaction postoperatively under two doses of ergotamine.

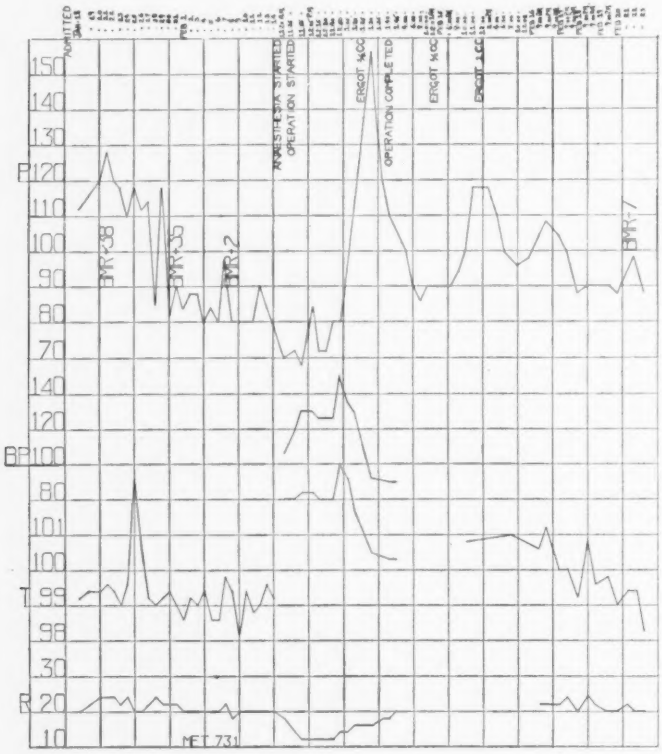

CHART 5.—Met. Hosp. No. 731: Shows the effect of ergotamine. ¼ mg., administered when pulse rate was 156; 20 minutes later, it had dropped to 100. Two postoperative doses of ergotamine maintained a fairly level postoperative plateau.

Discussion.—In 1913, Forcheimer[14] suggested the use of quinine and ergot in thyrotoxicosis in the preparation of patients for operation. Merke[15] recommended the use of ergotamine for the postoperative tachycardia following thyroidectomy, and reported several cases with beneficial results. This is the only reference to the use of ergot alkaloids in the surgical care of thyrotoxicosis noted in the literature and, as already mentioned, is concerned only with the postoperative period.

The medical treatment of thyrotoxicosis by means of ergotamine has had considerable application, but it would seem with rather indifferent results.

The first extensive clinical use of ergot alkaloids in the medical treatment of thyrotoxicosis was initiated by Adlersberg and Porges,[16] in 1924, and they reported,[17] in 1925, a series of cases with beneficial results following the use of the recently isolated ergot alkaloid, ergotamine. They reported another series of cases[18] in 1930, in which they showed a definite improvement in over one-half those treated. In 1931, Youmans and Trimble[19] reported some very interesting results. They found that the effect of ergotamine on the pulse rate was much more pronounced than the effect on the blood pressure. They, and others, report a slowing of the pulse in thyrotoxicosis which was more pronounced than in normal controls. The explanation for the lack of a more extensive application of this experience is probably, in part at least, dependent on the relative ease with which a tolerance develops. However, the potentiating action of thryroxin on adrenalin has not received from the surgeon or anesthetist the attention its essential and fundamental importance would seem to warrant. Some facts regarding this potentiating action seem worthy of mention.

Clark[20] gives some interesting statistics in this connection and makes the statement that adrenalin in a dilution of 1 in 10^{8}* gives certain characteristic and recognizable effects, but a similar result can be produced in a dilution of 1 in 10^{16}* if a solution of thyroxin 1 in 10^{16} is used as well. This being true, the potentiating effect of thyroxin on adrenalin must be enormous. These dilutions, however, are not so surprising as it may seem at first sight, when it is recalled that 1 cc. of a solution in a dilution of 1 in 10^{16} will, in the case of adrenalin, contain 300,000 molecules, and in the case of thyroxin 100,000 molecules. When these are distributed over the cells to be affected, it is obvious that an extremely small percentage of the cell surface could receive even a monomolecular layer of the drug, and this area where the drug is adsorbed may be spoken of as the pattern cell receptor. These figures may help to make comprehensible the efficacy of doses as small as those employed.

There is other evidence to suggest that such drugs as adrenalin, thyroxin, and ergotamine produce their effects by occupying cell receptors of a particular pattern with a monomolecular film. Andrus,[21] in 1932, and also Yater,[22] showed that hearts of thyroxinized animals continue to beat much longer *in vitro* than normal ones, and this effect persists for hours; this, of course, suggests an effect directly upon the heart muscle, whereas, when a heart is treated with atropine and adrenalin, the tachycardia subsides very quickly after being set up *in vitro*. However, reference should be made at this point to the fact that some observers do not accept the slowing of the pulse rate in mammals by ergotamine. For example, Dale[23] has shown that the efficiency of the cardiac accelerator antagonism by ergotamine is not too well established in mammals although the extreme results reported by Otto[24] have not met with substantiation. In any event, his results are subject to a different interpretation because the effect may not be a nerve mechanism at all, and Andrus

* The superior number of 10^{8} indicates one hundred million, and 10^{16} represents ten thousand million.

and Martin,[25] in dogs and cats, have obtained quite opposite findings. These authors have shown that when both vagal nerves were sectioned in the neck, and atropine given, the subsequent use of ergotamine still slowed sinus rhythm, and in their experience, subsequent injection of adrenalin failed to produce cardiac acceleration. They conclude that ergotamine produces effects without any relation to the vagus. Andrus and Martin[26] also showed that auriculoventricular conduction is depressed by ergotamine, with delay of transmission of excitatory processes in the auricle as shown by prolongation of the P—R interval in the electrocardiograph. Baur[27] has shown that ergotamine antagonizes the effect of adrenalin on the amniotic membranes of a goose's egg, which is totally lacking in nerve elements and, therefore, must represent a drug to muscle cell receptor mechanism of some kind. Rothlin[28] has shown that the heart of ergotaminized animals is more sensitive to vagal stimuli than is that of the controls.

In 1930, Matthes[29] showed that ergotamine has a specific inhibiting action on cholinesterase, but this is not nearly as sensitive, or as intimate, as that of eserine, nor will it work in equally extreme dilutions. This strongly suggests that ergotamine, by its action on cholinesterase, delays the destruction of acetylcholine and, hence, markedly potentiates vagal effects. Rake and McEachern[30] have shown that signs of hyperthyroidism in animals appeared only 36 to 48 hours after medication was begun. This is important, because any excess thyroxin appearing during the operative procedure could not explain the concomitant rise in pulse rate. Moreover, Collip[31] states that it is impossible to show an elevation of the basal rate after thyroxin therapy before ten to 12 hours. Rake and McEachern[32] also show that thyrotoxicosis in animals produces a decreased myocardial glycogen, but the heart showed no specific anatomic lesion, even after long continued use of thyroxin. Weller *et al.*[33] have rather definitely shown that there is no particular or specifically recognizable, morphologic myocardial lesion in thyrotoxicosis in humans.

The various mechanisms in operation to cause tachycardia might be grouped under three headings: (1) Increased adrenalin outpouring as a result of central and peripheral stimulation. (2) Thyroxin potentiation of adrenalin pattern cell receptor relationship in the specific tissue or conducting mechanism of the heart. (3) The action of thyroxin itself on the heart. The action of ergotoxine and ergotamine should be useful in minimizing the action of the first two with little, if any, effect on the third. In addition the vagal potentiation of ergotamine plays a definite rôle in the control of the tachycardia. This follows from the ergotamine-cholinesterase relationship resulting in enzyme inhibition and consequent prolongation of acetylcholine action.

Other Effects of Ergotoxine and Ergotamine.—Youmans and Trimble[34] report no untoward effects in patients treated over quite long periods with ergotamine. According to Barger, the harmful effects of therapeutic doses of ergotamine in a small percentage of subjects consist of slight giddiness, feeling of frontal pressure in the head, weariness, sometimes pain and soreness in the muscles, less frequently nausea and very rarely vomiting.

This brief discussion of the literature suggests that the tachycardia of thyrotoxicosis is not a compensating reaction but appears to be rather a fortuitous and undesirable event. Clinical experience would seem to adequately substantiate this, as most observers concur that its presence, particularly if long continued, adds greatly to the gravity of the condition. In any event, regardless of the mechanism responsible for the beneficial results obtained with this therapy, the present investigation brings substantial clinical evidence that this tachycardia can be advantageously influenced during the surgical care of thyrotoxicosis by the ergot alkaloids, ergotoxine and ergotamine.

CONCLUSIONS

(1) The ergot alkaloids, ergotoxine and ergotamine, are definitely useful adjuncts to the surgical management of thyrotoxicosis.

(2) The pulse rate in these cases seems better controlled than a comparable series without ergotoxine-ergotamine therapy.

(3) Ergotoxine and ergotamine have no recognizable effect on the tachycardia of anoxia.

(4) A supplemental oxygen supply, especially postoperatively, is of the greatest value in the surgery of thyrotoxicosis.

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COEXISTING CARCINOMATA OF THYROID AND ABERRANT THYROID WITH REGIONAL METASTASES*

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Case Report.—L. C., white, female, age 23, unmarried, was admitted to the Medical Service of Beth Israel Hospital, July 7, 1938, suffering from bronchopneumonia of the right lower lobe. After this had subsided, the patient continued to have an irregular temperature ranging at times as high as 103° F. Diagnoses of infectious mononucleosis, typhoid, and typhus fever were entertained because of the associated symptomatology but were excluded by appropriate clinical and laboratory studies. Attention then was directed to an irregular, diffuse, chronic swelling in the right cervical region. This mass, which was first noted 12 years previously, when the patient was 11 years of age, had been growing slowly in size. Two years after onset hoarseness, irritative cough, choking sensations and dysphagia began. All symptoms had continued without interruption up to the present. A diagnosis of tuberculous lymphadenitis was made in 1935, and appeared to be supported by a roentgenogram of the chest, which at that time was stated to have revealed extensive thickening about the right hilar area and nodular infiltrations in both pulmonary fields. There had been no evidence of active pulmonary tuberculosis however, and the patient's general condition had always been satisfactory. Two months prior to admission an abscess, which had developed in the midst of the cervical swelling following the local injection of some solution by her family physician, was incised and drained. Because of the long-standing antecedent history of a mass, a biopsy was taken from the abscess cavity at the time, but was reported to reveal only "inflamed necrotic tissue." The wound healed without incident. The remainder of the past history was irrelevant.

Physical Examination.—On admission to the hospital, local examination revealed a chain of firm, painless, discrete and coalescing, globular masses extending along the right side of the neck, from the tip of the mastoid process to the clavicle. These masses, which paralleled the sternomastoid muscle, varied in diameter from one to three centimeters. The chain, in its lower third, overlapped the right lobe of the thyroid gland. The individual nodules were freely movable and were especially prominent immediately below the angle of the jaw. At that point also, they extended deeply toward the floor of the mouth. The overlying skin was not adherent except in the upper cervical region at the site at which the preexisting abscess had been drained. There was some asymmetry of the right side of the face, apparently the result of an old injury to the facial nerve. This followed the first of two operations for posttraumatic ankylosis of the right temporomandibular joint at the age of seven and 14, respectively. Healed transverse scars related to these operations were present in the submandibular and preauricular areas. Aside from moderate enlargement of the right lobe of the thyroid and displacement of the upper portion of the trachea to the left, there were no other significant local findings.

The febrile course subsided after four weeks without a definite diagnosis having been made, and in order to exclude the diagnosis of a localized form of Hodgkin's disease, one of the cervical nodules was removed for pathologic examination. The report, by Dr. Alfred Plaut, was as follows:

Pathologic Examination.—Gross: The specimen consists of a soft, cyanotic, encapsulated mass, measuring 3.3x3.1x2.2 cm. On cut-surface many glassy, grayish protru-

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sions with an average diameter of one millimeter and a number of larger indistinctly outlined yellow areas are seen.

Microscopically, the characteristic picture of papilloma of the thyroid was to be seen. The epithelium is mostly cuboidal. It is flattened in areas in which the stroma of the papillae is swollen. This stroma shows a variety of edematous and so-called hyaline changes. Varying degrees of metachromasia are seen in the stroma. Occasional small areas of calcification are noted. The stroma in some areas is inflamed; while in others, foreign body giant cells surround the crystal spaces. Small glandular areas resemble thyroid tissue. The adjoining lymph node tissue shows nothing unusual. *Pathologic Diagnosis:* Papilloma of thyroid (watch for recurrence).

In view of the fact that this nodule had been situated at a point quite far lateral to, and well above, the thyroid gland it seemed logical to assume that it did not constitute a portion of the gland proper but represented a tumor situated within aberrant thyroid tissue.

FIG. 1.—Photomicrograph of a regional lymph node, identified by presence of normal lymph follicles (indicated by arrows). Note invasion by papillary carcinoma (metastatic). (Low power)

On September 23, 1938, the patient was transferred to the Surgical Service and operated upon, under the diagnosis of benign papillary tumor of aberrant thyroid tissue. Avertin, gas-oxygen-ether anesthesia were employed. Through a typical Kocher incision, the ribbon muscles were separated in the midline and retracted laterally. On exploration, the left lobe of the thyroid gland was normal, the right lobe was enlarged about 50 per cent. The major portion of the latter was occupied by a rounded, firm, discrete, grayish-yellow tumor which measured about three centimeters in diameter. Attached to it, and extending downward behind the clavicle, was a chain of similarly rounded nodules ranging in diameter from one-half to three centimeters. Many of these nodules were in close relation to the lateral wall of the trachea and esophagus. A number of small, normal lymph nodes were noted among the tumor masses. Firmly wedged in the superior thoracic aperture, displacing the trachea far to the left side, and resting on the dome of the pleura, was a large nodule measuring about four centimeters in diameter. Extending upward from the right thyroid lobe, beneath the sternomastoid muscle and surrounding the carotid sheath, was a similar chain of tumor masses and lymph nodes.

In order to expose the lesion to its upper limit, the existing incision was curved upward and carried along the anterior border of the sternomastoid muscle almost to the mastoid process. The tumor masses, which ended at the lower border of the parotid gland, were found firmly attached to the carotid sheath and at a number of points appeared to infiltrate the overlying muscle. Beneath the ramus of the mandible, the masses extended mesially to the floor of the mouth and the hyoid bone. In the upper half of the operative field, there was considerable scarring as the result of three previous operative procedures (submandibular arthroplasty, incision of abscess, and biopsy).

The right lobe of the thyroid first was widely resected. This was followed by the excision of all visible tumor masses and lymph nodes, together with a considerable quantity of surrounding fat, upward to the lower border of the parotid gland and downward to the dome of the pleura. Neither the carotid artery nor jugular vein were sacrificed as these structures did not appear to be infiltrated and could be dissected free without undue difficulty. At the conclusion of operation, the right side of the trachea and esophagus and the carotid sheath were quite bare. A small gauze wick was placed down to the retroclavicular dead space and brought out through a stab wound behind the lower portion of the sternomastoid muscle. A second gauze wick, placed alongside the wall of the pharynx was brought out through the same stab wound. The ribbon muscles then were approximated in the midline, and the subcutaneous tissues united with interrupted sutures. The skin was closed with clips.

Sections taken from various parts of the specimen, including the right lobe of the thyroid, regional lymph nodes, and the lateral cervical nodules, were reported by Doctor Plaut as follows:

Pathologic Examination.—Microscopic: "Most of the sections reveal the picture of papillary tumor as described in the previous biopsy specimens. Some of the papillary masses are situated in almost entirely destroyed lymph nodes. There is one piece of nontumorous lymph node. Occasionally, small areas of nonpapillary or only slightly papillary adenocarcinoma are seen." *Pathologic Diagnosis:* "Papillary malignant tumor of thyroid and aberrant thyroid, metastasizing in lymph nodes."

The postoperative course was entirely uneventful, the wound healing by primary union. A prophylactic course of radiation, advised by the Department of Radiotherapy, was commenced on the tenth postoperative day and continued in the Out-Patient Department following the patient's discharge from the hospital. Follow-up examination at the present time, 14 months after operation, reveals the operative wound to be well healed. There is no evidence of local recurrence or distant metastases. Roentgenologic examination of the chest is negative, and the trachea, which formerly was displaced toward the left side of the neck, is now in the midline. The patient has gained 14 pounds in weight, is in excellent general physical condition, and is entirely free of symptoms except for the persistence of some hoarseness. The latter is due to paralysis of the right vocal cord resulting from removal of a portion of the recurrent laryngeal nerve intimately involved in a mass of nodules alongside of the trachea and esophagus.

Discussion.—In a recent review of the thyroid material of the Cleveland Clinic, George W. Crile, Jr., stated that of 13 cases of papillary tumor of lateral aberrant thyroid tissue, five were associated with similar tumors situated within the thyroid gland proper. Cattell, also, has emphasized that in the presence of papillary lateral aberrant thyroid tumors, the thyroid gland proper is apt to contain one or more such lesions. The case which I have presented falls precisely into this group. In three of Crile's cases the thyroid tumor was considered malignant but in each instance the patient's course, following operation, has thus far been entirely satisfactory. Accordingly, Crile emphasizes that it is extremely difficult and at times impossible to distinguish between regional lymph nodes, invaded by metastatic papillary car-

cinoma arising in the thyroid gland proper, and multiple benign papillary tumors of aberrant thyroid tissue occurring concomitantly with benign papillary tumors of the thyroid gland erroneously considered malignant.

In the present case, the diagnosis of papillary carcinoma has been made independently by four pathologists. The evidence of malignancy of the tumor in the right lobe of the thyroid is not only its cellular structure but also invasion and infiltration beyond the limits of the capsule and into the connective tissue between the lobules. Another criterion is the presence of tumor tissue within structures which can be recognized readily as regional lymph nodes, the identity of the later being established by the presence of intact lymph follicles. The final evidence of malignancy is the presence of invasion of the capsule of certain large circumscribed tumor masses which represent either primary tumors of aberrant thyroid tissue or large lymph nodes whose structure has been grossly altered by extensive invasion of metastatic carcinoma arising primarily in the right lobe of the thyroid. The presence of a certain amount of lymphoid tissue within these nodules does not identify them as lymph nodes, since it is known that lymphoid tissue may be present normally in all lateral cervical embryologic anomalies such as cysts, sinuses, and aberrant thyroid tissue. There are, however, two features of the case which tend to establish the identity of the nodules in question, as of lateral aberrant thyroid origin. These are: First, the fact that the masses had been present for 12 years prior to operation (since the patient was 11 years of age); and second, that the wide distribution of the nodules from the mastoid process to the dome of the pleura would be most unusual for lymph nodes. A consideration of various clinical and pathologic features seems, therefore, to warrant the assumption that lateral aberrant thyroid tissue was present for many years; that papillary carcinoma developed in the right lobe of the thyroid gland and concomitantly in the aberrant thyroid tissue; and that the regional lymph nodes became involved by metastatic carcinoma from the thyroid gland tumor, or from the lateral aberrant thyroid tumors, or from both.

All authors appear to agree that papillary carcinoma of the thyroid and aberrant thyroid tissue is a highly differentiated, slowly growing lesion which exhibits a remarkably benign clinical course. Pemberton states that such a carcinoma may be present for a considerable period of time before invading the neighboring tissues and that, when nonencapsulated, it exhibits a predilection to spread to the regional cervical lymph nodes. Although the prognosis obviously is worse if there is regional lymph node involvement, it must be remembered that carcinomatous lateral cervical masses may represent lateral aberrant thyroid tissue involved by primary carcinoma and not regional lymph nodes involved by metastatic carcinoma. Even if the existence of the latter is established, as was done in the present case, radical removal is still indicated. Because of the high degree of differentiation of the tumor and its radioresistance, all observers now agree that pre- or postoperative radiation is of little or no value. If postoperative recurrence is noted, further operation rather than radiotherapy is indicated for the reason just stated.

PAPILLARY ADENOMA OF ABERRANT THYROID*

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TUMORS of aberrant thyroid, which appear as papillary adenoma or adenocarcinoma, are relatively uncommon. George Crile, Jr.,[1] in a recent paper reviewing 17 cases from the Crile Clinic, stated that, including his own, 136 cases had been reported in the literature to date.

Case Report.—E. L., male, age 24, was admitted to St. Luke's Hospital in October, 1939, complaining of swelling on both sides of the neck, recently increasing on the left. This had first been noted about ten months previously. Six months ago, at another hospital, a biopsy from the right side of the neck was obtained and a diagnosis of papillary carcinoma, probably orginating from the thyroid, was made. He was given two courses of radiotherapy to the neck without relief. Operation was advised but not accepted at that time.

On examination, although thin and delicate in appearance, he was not acutely ill. There were firm masses suggesting enlargements of the nodes on both sides of the neck along the sternomastoid muscles. On the right side they extended to the level of the angle of the jaw above. On the left the base was lower and broadened out laterally just above the clavicle. The thyroid did not seem enlarged but small hard nodules were palpable in the isthmus. Roentgenologic examination revealed a mass in the upper mediastinum pushing the trachea somewhat to the left. The basal metabolism was ± 0.

The right side of the neck was operated upon, October 18, 1939, through an incision along the sternomastoid muscle. Two firm masses lying in a vascular, areolar tissue between the muscle and the internal jugular vein were removed. The thyroid gland was not exposed satisfactorily through this incision, nor could a mediastinal mass be felt.

During the operation, which was performed under colonic ether, the patient's breathing was continually obstructed, and after he was returned to the ward he became so cyanotic that it was necessary to introduce an intratracheal tube. In this connection, it is interesting to note that on the day after his biopsy, six months previously, the patient was said to have become suddenly extremely cyanotic, and breathing to have stopped, requiring artificial respiration and stimulants.

A second operation was performed November 3, 1939, under intratracheal anesthesia. At this time the usual thyroid incision was made. The mediastinal mass, below and distinct from the right lobe of the thyroid gland, proved to be an aberrant thyroid extending from the right side of the trachea and posteriorly to it. It was removed with some difficulty. The isthmus of the thyroid and the anterior inferior portion of the right lobe were found to contain tumor, identical on frozen-section with that of the aberrant tumors, which extended downward on the front of the trachea. After its removal, the presumably normal left lobe and upper one-third of the right lobe of the thyroid remained.

A third operation was performed November 17, 1939. As the mass in the lower left neck extended so far laterally, it was thought better to approach it through a transverse rather than oblique incision. Consequently, two transverse incisions were made. Through the upper one, a mass was removed from underneath the sternomastoid muscle at about the level of the hyoid bone and through the lower two masses, one solid the other cystic in part, lying mainly under the clavicular origin of the muscle. Gas

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anesthesia, without an intratracheal tube, was employed for this operation, with no respiratory difficulties. *Pathologic Diagnosis:* Papillary adenoma of aberrant thyroid and thyroid.

Points of interest are involvement of both sides of the neck, which was found in five of Crile's 17 cases, simultaneous involvement of the thyroid, found in eight of Crile's cases, and the mediastinal location of one tumor causing pressure on the trachea and interference with breathing. Crile reported a mediastinal tumor in five of his series.

FIG. 1.—Tissue removed from Case E. L. Lower, center mediastinal mass. Just above it tumor removed from thyroid.

The question of greatest importance in these tumors is that of malignancy. About one-third of those reported are classified as carcinomata. The late results indicate, however, that the grade of malignancy, when present, is low.

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DISCUSSION.—DR. CHARLES GORDON HEYD (New York) called attention to the well-established fact that certain types of heart disease associated with hyperthyroidism exhibit rather miraculous cures after surgical intervention. The unfortunate part of heart disease in goiter is that most of these patients come to Cardiac Clinics for their disabilities, where they are treated for an indefinite time before being submitted to the beneficent effects of surgery. When told eventually that their cardiac condition is in a large measure due to their goiter condition, they express great surprise and state that they have not had a goiter for many years and that it has given no trouble. It is sometimes very difficult to convince them that the heart disease is largely due to a goiter that apparently gave no symptoms. Yet the effort must be made, because, as illustrated by Doctor Smith's case, there are few individuals, in the

field of cardiac pathology, who can be so improved by surgery as the patient with cardiac symptoms due to hyperthyroidism.

DR. ARTHUR P. STOUT (New York) described the experiment undertaken at the Presbyterian Hospital with tumors of the lateral aberrant thyroid. Before doing so, however, he quoted Doctor Crile as follows: "It has not been proved that either distant or local metastases occur from papillary tumors of lateral aberrant thyroid origin." Furthermore, "none of the 13 patients in this series has died as a result of lateral aberrant thyroid disease. . . ." and, speaking of papillary tumors of the thyroid gland, Chile has said: "In no instance has it been proved that either regional or distant metastasis took place."

At the Presbyterian and Babies Hospitals, there have been 22 cases of lateral aberrant thyroid disease designated as follows: Simple hypertrophy, one case. Adenoma, five cases. Benign papillary tumor, three cases. Carcinoma, thirteen cases. Of the carcinomata, ten were of the papillary type, three of the solid type. Of the 13, three were males, ten females. Seven of the 13 had tumors in the thyroid, also; two of them had bilateral involvement—just as Doctor Smith's case had. One four-year-old child had bilateral involvement, with a nodule in the thyroid, also. The other case had no nodule in the thyroid but tumors in both sides of the neck.

In regard to lymph node metastasis, in order to accept the occurrence of metastasis, inasmuch as the lateral thyroid nodules have lymphoid tissue in them, it is necessary to find the actual structure of the lymph node with its sinuses and its follicles. In order to determine whether or not those nodules which had been called metastases fulfilled the criteria, Doctor Stout recently reviewed the cases mentioned and found that six cases did have isolated papillary growths in unmistakable lymph nodes. Therefore, he felt that metastasis can occur in lateral, aberrant thyroid, malignant tumors. As to the results in these cases: Three of the 13 carcinoma patients have died—two with local recurrence and one with lung metastases. Hence, like other malignant tumors, carcinoma of the lateral aberrant thyroid may have a fatal outcome. Three of the patients are alive, at various periods, up to eight years, after the operation, with local palpable nodules. Whether or not these are cases of persistence of the tumor or newly developed lateral thyroid nodules, Doctor Stout could not specify. Seven are well, but only two of the seven have been well more than three years. There have been a number of these cases during the last two years.

In contradistinction to Crile's statement that metastasis from papillary tumors of the thyroid never occurs, Doctor Stout said that in going over the tumors of the thyroid at the hospitals mentioned, he found that four cases of papillary carcinoma also had metastases in lymph nodes. Therefore, in Doctor Stout's experience, although it is perhaps the least malignant of the thyroid tumors, papillary tumors are not without some threat to life.

DR. FRANK B. BERRY (New York) described a case that he had had with multiple aberrant foci in the neck, right lobe of the thyroid, and mediastinum 28 months ago. All were removed including complete removal of the right lobe and isthmus, with suspicious nodules in the right lobe reported as normal thyroid. The patient is well. She was 19 years old at the time of operation, and the condition was first noticed when she was 12 years old. She had been under the care of an internist in the interval period and these masses were thought to be tuberculous lymph nodes. Two or three months before she came to Doctor Berry they had begun to increase in size.

Dr. Herbert Willy Meyer (New York) said that he, too, had operated upon a case of papillary adenocarcinoma occurring in an aberrant thyroid. The patient was a woman, age 55. The tumor was in the outer portion of the right side of the neck, about the size of a walnut, and was freely movable. There were no palpable lymph nodes. Careful nasopharyngeal examination was negative and roentgenologic examination of the chest was also negative. Two aspiration biopsies had been performed at another hospital, but the patient stated that no definite diagnosis could be made. She was operated upon, December 13, 1937, at the Lenox Hill Hospital. Pathologic examination revealed a typical papillary adenocarcinoma occurring in aberrant thyroid tissue. The mass was easily removed, being encapsulated. She made an uneventful recovery, and is entirely well two years since operation.

From the few cases previously reported before the New York Surgical Society, this condition could be considered quite rare. But in view of the large number of cases cited at this time from various clinics, one must change his point of view and consider it to be much more frequent.

The first case presented before the New York Surgical Society was on May 10, 1910, when Dr. Eugene Pool reported upon a patient operated upon by Dr. Frank Hartley. This was a papillary carcinoma in an aberrant thyroid with definite lymph node metastasis. In 1914, Dr. Walton Martin reported a similar case; then there was no further report until 1926, when Dr. Richard Lewisohn reported a case of bilateral, symmetrical aberrant thyroids. The last previous report was in 1930, when Dr. Seward Erdman reported an adenocarcinoma of aberrant thyroid tissue occurring within the parotid gland.

Doctor Meyer showed a lantern slide depicting a reconstruction model of a human embryo, made in 1906, by the Russian surgeon, Wenglowski. It showed how the thyroid tissue comes down from the foramen cecum in the thyroglossal tract to form the isthmus and the main body of the thyroid gland. The lateral lobes develop from the epithelial pocket in the floor of the fourth pharyngeal pouch. A more detailed description of this may be found in an article published by Doctor Meyer entitled "Congenital Cysts and Fistulae of the Neck," in the February, 1932, issue of the Annals of Surgery. It is, undoubtedly, from the lateral remnants of thyroid cells that these tumors of aberrant thyroid tissue develop. They are usually outside the internal jugular vein or may lie just in front of it.

It must not be forgotten that aberrant thyroid tissue can also be present in other parts of the body. Billings and Paul, quoted by Cattell, from the Lahey Clinic, in 1931, reported 34 authentic cases collected from the literature from 1857 to 1923. Cattell reported 13 additional instances. In the world literature, however, there are numerous reports of aberrant thyroid tumors; on the average about 12 cases a year for the past ten years. These were both benign and malignant. The greatest number occurred at the base of the tongue. The second most frequent location, as reported, is in teratoma of the ovary.

Doctor Meeker, of the New York Post-Graduate Hospital, has collected a group of cases from that hospital, in which aberrant thyroid tissue has been found at the outer ends of the clavicle, in the pineal gland within the brain, within the brain itself (several cases), in the testes and in the prevertebral area within the abdomen. In the literature, one finds that aberrant thyroid tumors have also been found in the long bones, skull, pericardium, pleura, intratracheal, intralaryngeal, retropharyngeal, within the lungs and in the retina of the eye.

One and one-half years ago, Doctor Meyer operated at the Post-Graduate Hospital upon a case in which the pathologists finally agreed that the tumor

was probably a primary carcinoma of aberrant thyroid tissue occurring in the intercostal structures on the left side of the chest. A resection of the chest wall was performed. The patient did not have a local recurrence, but died one year after operation from what was believed to be a spinal metastasis with paralysis. Unfortunately, an autopsy could not be obtained.

One important point to remember is to try and determine the presence of a normal thyroid gland in its normal location if one suspects a tumor of aberrant thyroid tissue. Cases are reported in the literature in which myxedema developed after the removal of aberrant thyroid tissue, the tissue probably being the only thyroid tissue present.

SUBSTERNAL THYROID*

WILLIAM B. PARSONS, M.D.
NEW YORK, N. Y.

Case Report.—U. H. No. 567901: A. H., white, male, age 55, surgeon, was admitted to the Presbyterian Hospital, December 11, 1938. His previous and family histories were irrelevant, except for the fact that one year previously, having had some precordial distress, an electrocardiogram was made which was found negative. A roentgenogram of the chest at that time revealed a large, intrathoracic goiter on the right side, with deviation of the trachea to the left. He was busy, and so relieved by the negative electrocardiogram report that he postponed action on the goiter, which had given no symptoms of any kind.

Five months before admission, gradually increasing hoarseness appeared, which, one month before admission, had assumed major proportions. At times he was completely aphonic; and at all times his voice was not much better than a hoarse whisper. Laryngeal examination by various examiners could be summarized as follows: The right cord and arytenoid were in the midline, and immobile. The left cord and arytenoid were usually noted in the cadaveric position, and exhibited but little motion.

Temperature, pulse, respiration, blood pressure, and physical examination in general were all negative, except for a firm mass, palpable just above the right clavicle, which obviously continued below that level.

Here was a patient, then, who presented a large intrathoracic goiter, with not only an ipsolateral paralysis but a marked contralateral weakness of the vocal cords.

The possibility of carcinoma was, of course, seriously considered; but the lung fields were innocent of any shadow suggesting metastasis.

Operation.—Under cyclopropane by the intratracheal route, the left lobe was found to be soft and apparently normal, as was the upper part of the right lobe. A large, nodular mass, about 13 cm. in length and about 8 cm. in diameter, arose from the lower part of the right lobe, and extended well down into the thorax. The depressor muscles were divided; the superior and inferior vessels were ligated on the right side; and the isthmus divided. Most of the right lobe was excised; and although the vascular supply to the intrathoracic mass had been controlled, it was impossible to deliver the tumor, because of the disparity in size between it and the superior aperture of the thorax. There seemed to be no evidence of infiltration into the surrounding tissues, strongly suggesting that the mass was not carcinomatous. Therefore, the dome of the tumor was removed, and a large amount of the central portion of the tumor was scooped out. Several curved clamps were then applied, one blade inside and one outside of the capsule; and it was then possible, by traction on the clamps, and with finger and sponge stick, to deliver the mass from the thorax. When the mass was delivered, it was a simple matter to remove it. Study of the field revealed the presence of parathyroids in place, and the right recurrent nerve was identified. The incision was closed without drainage.

The patient made an uneventful convalescence, and was discharged on the seventh postoperative day.

His present condition, 11 months following operation, is very satisfactory. A roentgenogram shows the trachea in the midline; and examination of the vocal cords shows that they both function as if normal.

This case is shown as an unusual example of bilateral, recurrent nerve

* Presented before the New York Surgical Society, November 22, 1939. Submitted for publication February 21, 1940.

palsy due to intrathoracic goiter, with complete restitution of function following operation. I confess that I cannot explain the exact mechanics of either the ipsolateral or contralateral paralysis. The contralateral type exists often enough to make it essential to determine, in any given case with vocal cord weakness, whether it is the nerve on the same or on the opposite side that is involved. This case also demonstrates the value of scooping out the central portion of a mass that is too large to deliver from the thorax; and it is suggested that the application of several curved clamps to the capsule is a good method of applying traction in some of these difficult procedures.

DISCUSSION.—DR. RODERICK V. GRACE (New York) remarked that the complication that occurred in Doctor Parsons' patient is a very rare one. Unilateral root nerve paralysis has been reported as frequently as occurring in 15 per cent of total intrathoracic goiters. Bilateral paralysis, however, is so rare that Doctor Grace could find only one other case similar to that reported by Doctor Parsons, which had been reported by Dr. George M. Curtis, of the Billings Clinic, in 1931.

DR. CARL EGGERS (New York) cited a case of intrathoracic or mediastinal goiter.

Case Report.—Mrs. V., age 55, was admitted to Lenox Hill Hospital, February 26, 1939, with the diagnosis of mediastinal tumor, probably malignant. Her outstanding symptoms were dyspnea, cough, cyanosis and loss of 40 lbs. in weight. There was a history of an old heart affection of many years' duration.

Physical Examination.—The patient was a small, rather stout woman, weighing 118 lbs., with a short, thick neck. There was a spinal deformity which projected her head forward and made examination difficult. Cyanosis and the presence of greatly dilated veins over the anterior chest were the outstanding findings. The presence of a nodule in the thyroid, a pulse of 120, and the marked loss of weight called attention to the possibility of a goiter. A roentgenogram of the chest showed a tumor in the upper mediastinum. Basal metabolism, plus 53. She was a poor operative risk on account of her heart disease and the deformity of her neck. For this reason, she was placed under the care of a cardiologist and a course of roentgenotherapy was administered. There was absolutely no improvement. Operation seemed to offer the only hope of relief.

Operation.—Under local anesthesia, a subtotal thyroidectomy was performed, which was very difficult on account of the awkward position of the head. A large, nodular goiter was found. There was no extension into the thorax, and with the palpating finger no tumor mass could be felt in the mediastinum. We revised our opinion and thought we were dealing with two conditions. However, when no improvement resulted, when her pulse rate remained high, the basal metabolism continued unchanged, and the radiographic examination showed a persisting mediastinal shadow, it was decided that the condition was best explained on the basis of an aberrant thyroid. On account of the severity of the pressure symptoms its removal became imperative.

Second Operation.—Under local anesthesia, the entire manubrium was resected. Both pleurae were exposed but not injured. A large, nodular tumor occupied the entire upper mediastinum, firmly compressing the trachea. It had to be removed in pieces, which was accomplished without injury to other structures, and without bleeding. The patient stood the operation well and felt so relieved that a satisfactory result was expected. However, she developed a very acute, fulminating hyperthyroidism which resisted all measures to combat, and led to a fatal outcome after about 30 hours.

In summary, the patient was one in whom pressure symptoms, rather than toxic symptoms, predominated, but in whom acute hyperthyroidism caused

death. The gross as well as the miscroscopic pathology of the cervical and the mediastinal thyroid was identical, and showed degenerating colloid and hyperplastic goiter. There were no evidences of malignancy.

DR. A. HOLZMAN (New York) said that inasmuch as he was the patient who had possessed this unusual condition, he felt that a few personal remarks about symptomatology and outcome might be of interest. The first symptom was precordial pain that was not brought on by any effort but was almost continuous. Whether lying down, sitting up or standing, whether exerting himself or not, Doctor Holzman said the amount of pressure directly over the trachea was of a certain intensity. The last symptom to develop was intermittent hoarseness. At times his voice was normal; again, there was complete aphonia. This situation was very embarrassing because it prevented the carrying on of one's work. The type of anesthesia employed at operation was ideal; there was no pain during, immediately, or some time after the operation, and the end-result is excellent. Doctor Holzman said that his voice had fully returned to normal, even to such an extent that he is able to resume singing as a tenor in a choir.

AN OSTEOPLASTIC NEUROLYSIS OPERATION FOR THE CURE OF MERALGIA PARESTHETICA

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BALTIMORE, MD.

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THE PURPOSE of this article is to present, for the cure of severe cases of meralgia paresthetica, an operation which is apparently new. In the past, resection of the lateral femoral cutaneous nerve has been the operation of choice. But even this radical measure has not always been successful (Bramwell[1]). The causes for failure were: (1) Formation of a neuroma at the proximal end of the divided nerve; (2) resection too far distal to the inguinal ligament; and (3) mistaken diagnosis, in that the lateral femoral cutaneous nerve was secondarily involved either because of an inflammatory process originating in an organ adjacent to its course, such as appendicitis, or because tumors pressed on the nerve. Again, it must be remembered that resection of the lateral femoral cutaneous nerve produces complete anesthesia over the lateral aspect of the thigh. The ideal treatment, therefore, would be one which not only relieves the patient of his pain but also restores to him normal sensation in the involved area.

Case Report.—J. W., white, male, age 46, was admitted to the Johns Hopkins Hospital, February 16, 1936, suffering from pain and numbness in the right thigh.

Previous History.—About five years before admission he noticed numbness in the skin of the outer part of his thigh immediately above the knee. Pain gradually appeared in the numb area, and the hair in this region became scant and short. Hyperextension of the thigh was constantly necessary in his work, and he found that this form of exertion was conducive to the production of the pain which was burning in character. The mere rubbing of his clothes on the affected part of his thigh also frequently produced the pain. Massage, hot compresses, salves and ointments were used without much benefit. Complete rest in bed was the most helpful measure. Because the pain was constantly increasing in severity, hampering him at his work, and causing much loss of sleep, he applied for relief.

Physical Examination.—Except for the sensory disturbance of the right thigh, the examination was essentially negative. The patient was five feet eight inches tall, of very muscular build, and weighed 175½ pounds. The lateral aspect of the right thigh was apparently normal in appearance except for the hair which was sparse, short, and brittle in the area marked T in Figure 1. This figure also shows the extent of other sensory disturbances, and covers, fairly well, the cutaneous distribution of the entire lateral femoral cutaneous nerve. Firm pressure on the nerve at the anterior superior spine of the ilium was not painful. The left thigh showed no sensory changes.

Laboratory Data.—Blood pressure 115/68; hemoglobin 100 per cent; white blood cells, 11,000; Wassermann reaction negative; van den Bergh negative; basal metabolic rate plus 7.

Operation.—February 18, 1936: Under avertin and gas-oxygen anesthesia, the right lateral femoral cutaneous nerve was exposed through a transverse incision which was

Submitted for publication June 6, 1939.

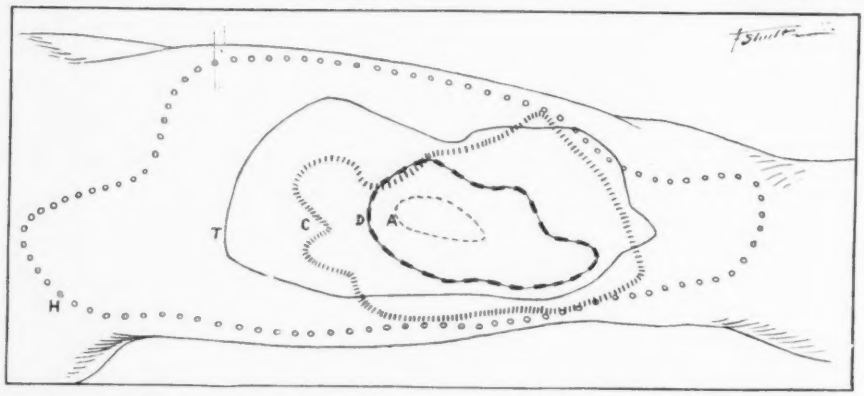

FIG. 1.—February 17, 1936. Patient J. W.: Lateral aspect of right thigh: Sensory disturbance of skin before simple neurolysis of the lateral femoral cutaneous nerve on February 18, 1936. Legend for this and all other sensory charts: (A) Area of complete anesthesia to pin prick; (D) area in which the pin prick is experienced as a dull sensation; (C) area in which the sensation of cold is not recognized; (H) area in which the sensation of heat is not felt; (T) area in which the sensation of light touch (wisp of cotton) is not perceived.

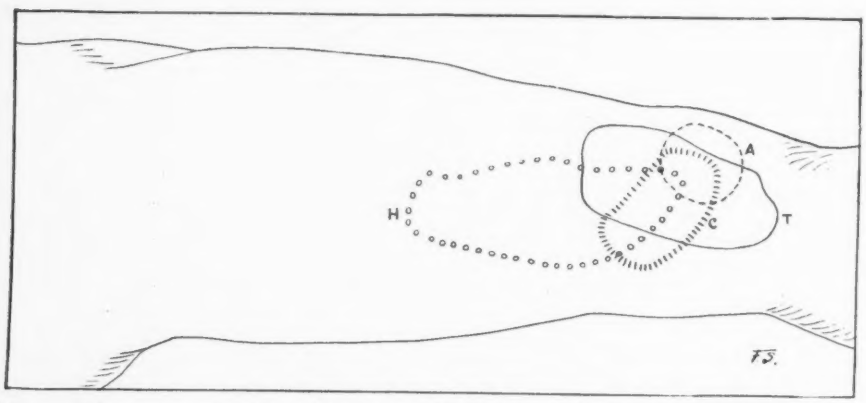

FIG. 2.—February 19, 1936. Day after operation: Note the extensive improvement. There is much overlapping of the sensations.

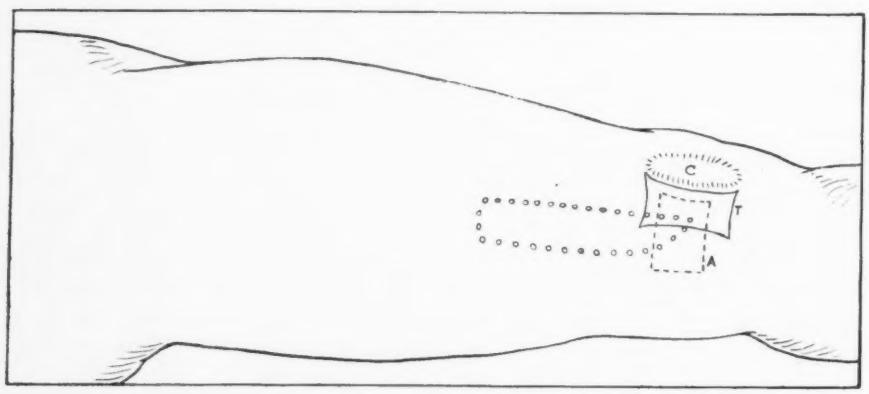

FIG. 3.—February 20, 1936: Improvement continues at almost the same rate.

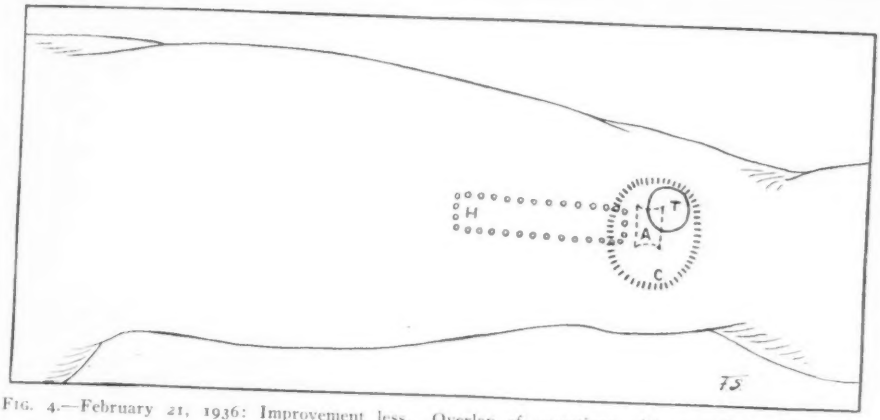

FIG. 4.—February 21, 1936: Improvement less. Overlap of sensations with a marked shift in the "cold" area.

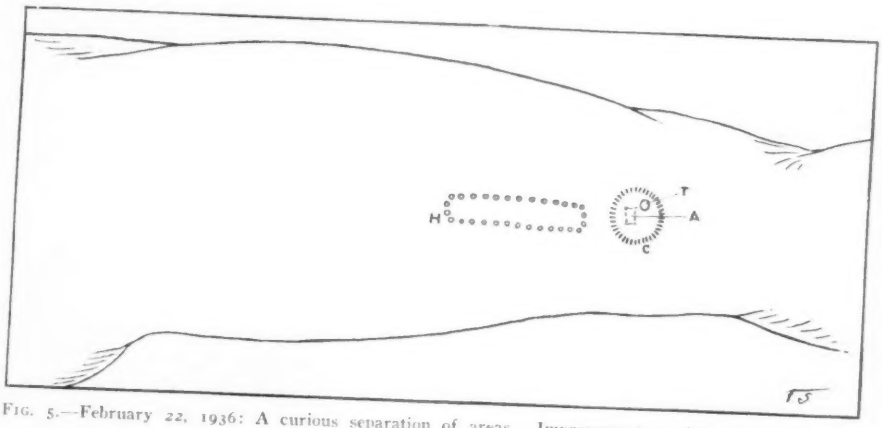

FIG. 5.—February 22, 1936: A curious separation of areas. Improvement continues but at a much slower pace.

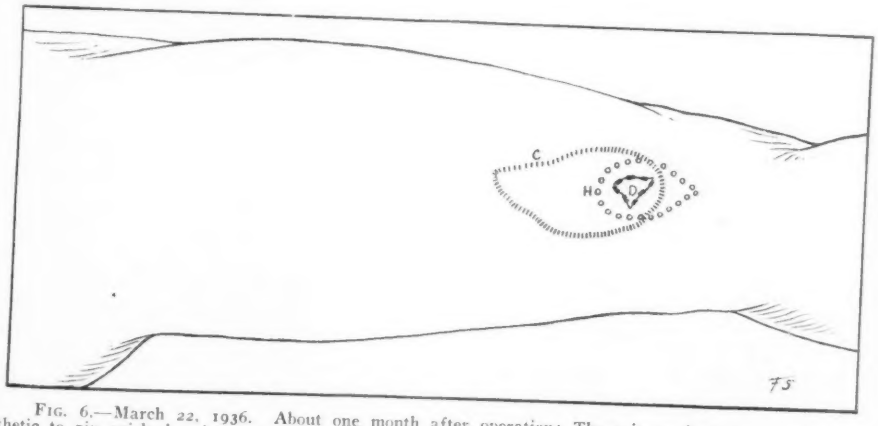

FIG. 6.—March 22, 1936. About one month after operation: There is no longer an area anesthetic to pin prick, but improvement seems to have been arrested. The "cold" area is much longer. There is no overlap.

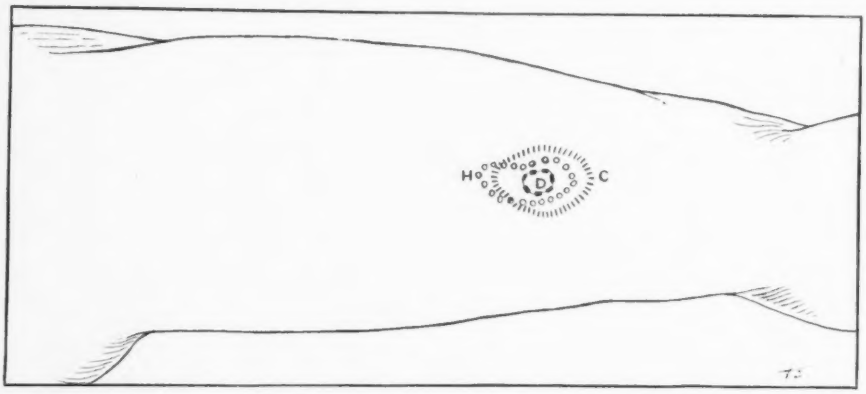

FIG. 7.—May 24, 1936: Still some improvement, but occasional pains were still present.

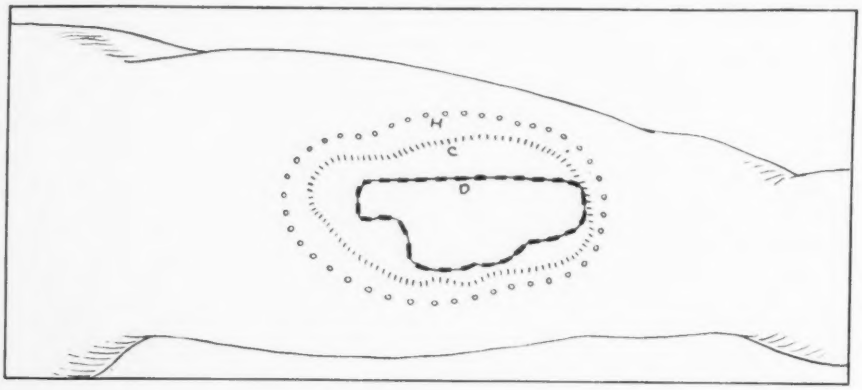

FIG. 8.—October 4, 1936: Sensory changes much worse. Shooting and burning pains more intense.

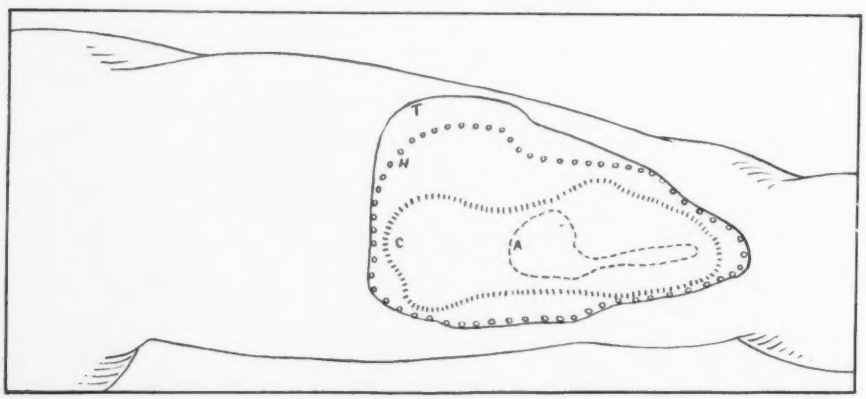

FIG. 9.—November 30, 1936: Condition still worse. An area of anesthesia to pin prick has appeared. There is no overlap of sensations. Pains were severe and almost prevented him from working. (Compare with Figure 1.)

made slightly below the anterior inferior spine of the ilium. The nerve was compressed for a distance of 0.5 cm. under the inguinal ligament. Above and below this constricted area the nerve was 2.7 Mm. wide and 1.2 Mm. thick, whereas at the compressed area it was 1.7 Mm. wide and 0.8 Mm. thick. All measurements were made with calipers. The nerve was thus compressed to 40 per cent of its normal size. In freeing the nerve, it was necessary to cut the lower fibers of the inguinal ligament, but, even then, only the tip of the index finger could be inserted between the nerve and the underlying bone. Since such a simple neurolysis had cured a previous case, a simple closure of the subcutaneous tissue and skin was undertaken.

The patient was not in condition to respond accurately to tests on the afternoon of the day of the operation, but those made during the four subsequent days showed daily improvement (Figs. 2, 3, 4, and 5).

Subsequent Course.—About one month later, March 22, 1936, after having worked for two weeks, stiffness and a mild burning pain began to return. Rainy weather made the condition worse. Sensory changes are shown in Figure 6.

About three months after operation, May 24, 1936, a sensory examination (Fig. 7) showed small improvement. He continued to work, but had occasional shooting pains.

During the following five months the burning pain gradually increased in frequency and intensity to such an extent that he again considered giving up his job. He was reexamined October 4, 1936, and it was found that his condition had become worse (Fig. 8).

This unfavorable course was considered parallel to that of the first patient[6] (H. H.), who gradually became worse after simple neurolysis until the seventy-second day, but subsequently improved and was completely cured eight and one-half months after operation, and has remained well now for over four years.

He returned to the hospital, November 30, 1936, complaining of much pain and disability. It was difficult to fall asleep. Sensory changes were less (Fig. 9) than on the first admission. The chief trouble was with the longest nerve fibers which went to the knee.

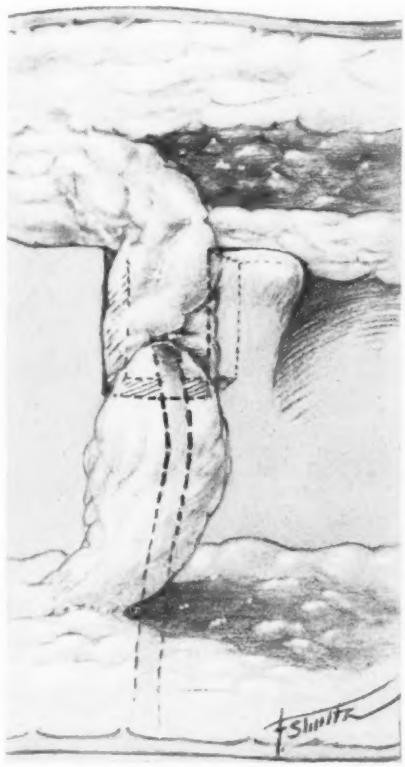

FIG. 10.—Drawing to show the main points in the osteoplastic neurolysis operation. A slot is cut in the crest of the ilium posterior to the anterior superior spine, and the lateral femoral cutaneous nerve (dotted outline), surrounded by fat pedicles, is placed into this new position. Pressure and tension can no longer exert force on the nerve.

It was decided to attempt another neurolysis operation because: (1) The immediate benefits of the first operation were striking; (2) there was still some improvement (compare Figs. 1 and 9); (3) the nerve had not received as much freeing as in the previous case; (4) his muscular build and type of work promoted fibrosis at the operative site; and (5) if neurolysis should fail again, then the nerve could always be resected.

The immediate problem was to devise an operation which would give more freedom to the nerve; put it under less tension; and surround it with fat in order that subsequent fibrosis and compression might be forestalled as much as possible.

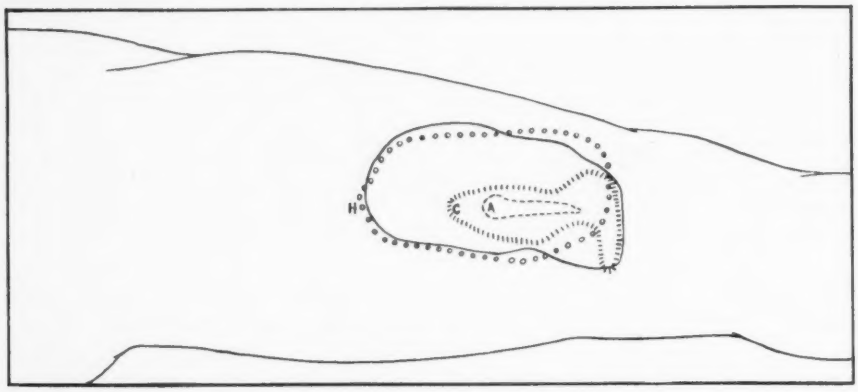

FIG. 11.—December 2, 1936. Day after osteoplastic neurolysis operation: Note again the marked sensory improvement.

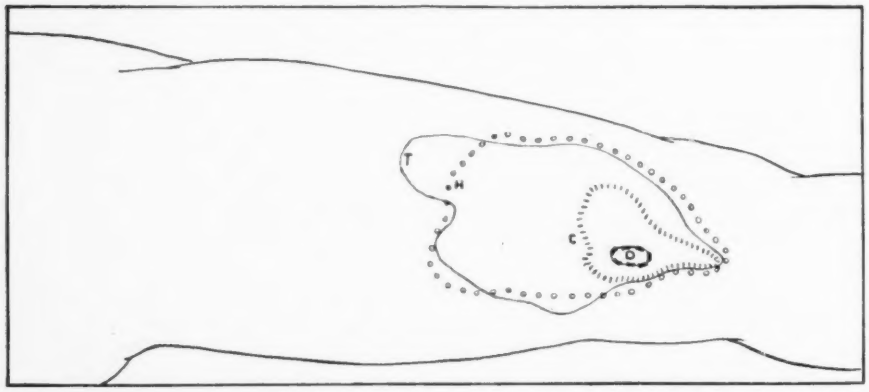

FIG. 12.—December 3, 1936: Condition temporarily worse. Note absence of anesthesia to pin prick.

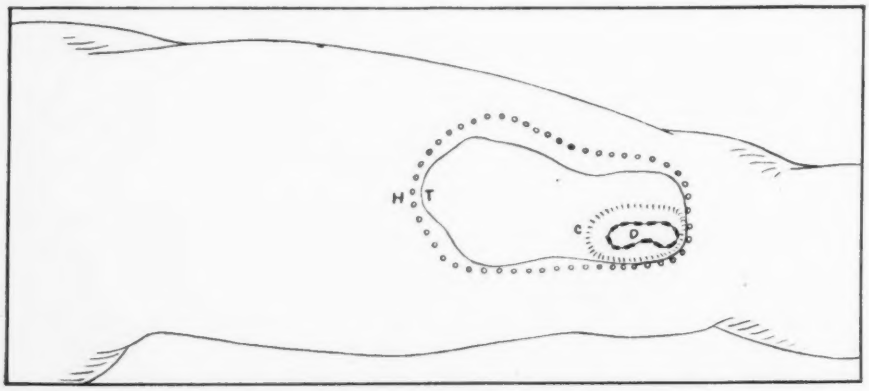

FIG. 13.—December 4, 1936: Not much change from previous day. No overlapping of sensory areas.

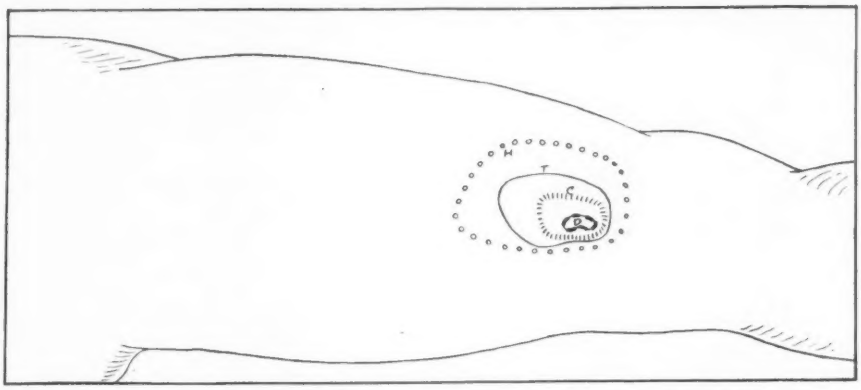

FIG. 14.—December 5, 1936: Very marked improvement, particularly to sensations of light touch and cold. (Compare with Figure 5 for the corresponding period after operation.)

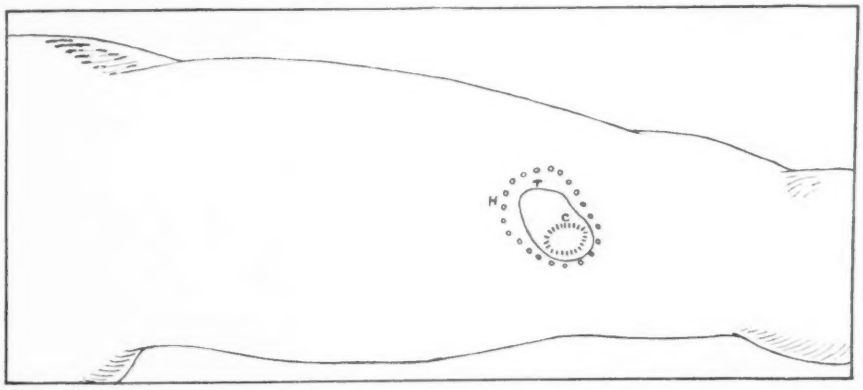

FIG. 15.—December 6, 1936: Further improvement.

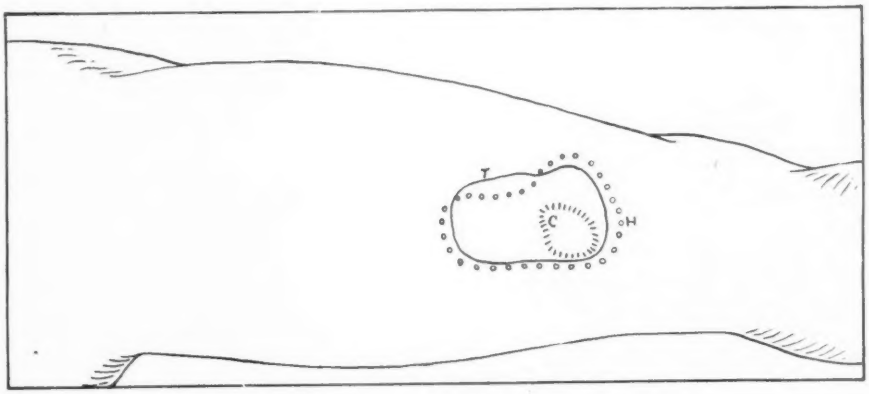

FIG. 16.—December 7, 1936: Condition temporarily worse.

Second Operation.—December 1, 1936: The chief point in the new operation was the cutting, with a rongeur, of a slot in the crest of the ilium one inch posterior to the anterior superior spine, and deeply enough so that the nerve, which was embedded in scar tissue, would be quite relaxed and would no longer be required to make a right-angled bend at the ilium. Figure 10 shows the completed operation with two pedicle fat flaps surrounding the nerve. Several interrupted silk sutures repaired the inguinal liga-

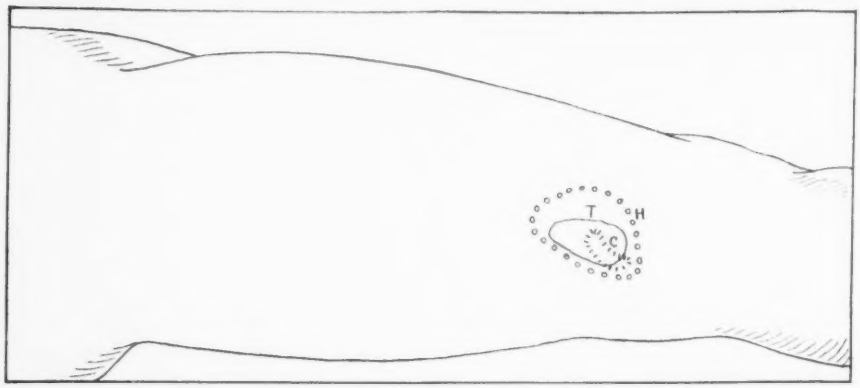

FIG. 17.—December 8, 1936: About the same as two days previously.

ment; the incision was then closed as before. A roentgenogram was taken of the ilium for a record.

Subsequent Course.—The patient was at once free of the burning pain, and the sensory improvements, day by day, are shown in Figures 12 to 17, inclusive. On the day of discharge, December 8, 1936, the two-point compass test showed the involved area to be one-half as accurate as normal skin.

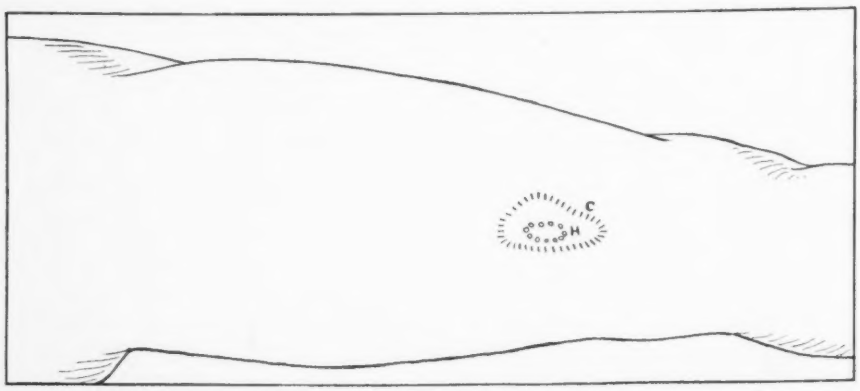

FIG. 18.—October 27, 1937: Almost complete normal sensations. Hot and cold are experienced in the above marked areas; however, the intensity of the sensation is less than normal.

He returned to work three weeks after operation, and continued to improve gradually. When examined October 27, 1937, more than 11 months after operation he was almost normal (Fig. 18).

December 11, 1938: Slightly more than two years after the second operation he was free of pain even if he hyperextended his leg. Physical examination showed that the hairs on the affected skin were about normal, and that there was no longer any sensory disturbance in skin of the previously involved area. A roentgenogram showed no change in the groove of the ilium when compared with that taken immediately after operation.

COMMENT.—Two cases of severe meralgia paresthetica have thus been relieved of their pain and have had normal sensation restored. Obviously, not much can be claimed on the basis of these two cases, but it must be remembered that severe cases of the disease are rare and that it, therefore, would take a long time to collect a sufficiently large number. That the condition is rare may be gathered from the article by Ecker and Woltman,[3] of the Mayo Clinic, who reported an incidence of all grades of severity of the condition of three in every 10,000 admissions.

The first attempt at a possible neurolysis operation was that of Neisser and Pollack,[7] in 1902, who cut the inguinal ligament over the femoral nerve; much later Learmonth,[4] in 1933, reported a very mild bilateral case which was relieved by simple neurolysis.

Why simple neurolysis cured the first patient[5, 6] (H. H.), and not the second may be explained on the basis that the first patient was large, fat, and with more slack in the nerve after neurolysis, thus allowing more opportunity for fat to surround the nerve at the ilium. However, in the second patient, whose history has been detailed above, there was very little room between the nerve and the bone after the first neurolysis operation, and it is reasonable to believe that the subsequent fibrosis again compressed the nerve. The sharp angulation of the nerve on crossing the ilium has previously been stressed by Stookey[8] as a cause for the disease; the experience gained from the second case indicates that compression of the nerve is, possibly, also a great etiologic factor.

Several objections have been raised to this new, modified neurolysis operation, which, for want of a better term, has been termed "osteoplastic." One is that the inguinal ligament must be cut at the anterior superior spine in order to transplant the nerve into its new location, and that this procedure may weaken the inguinal region enough so that a hernia may develop. In reply, it may be said that the patient whose inguinal ligament was cut has undertaken heavy manual work for over two years, beginning three weeks after operation, without any sign of a hernia or any other physical defect.

Another objection has been that the nerve in its new location may possibly be compressed by regenerating bone. This objection may be met by pointing out: (1) That the patient had a normally functioning nerve two years after operation, long after regenerating bone would have produced compression; (2) that a roentgenogram showed that bone was not filling in the slot into which nerve had been placed; and (3) that, experimentally, the radial nerve of a cat was placed in a groove of the humerus in such a manner that bone completely encircled the nerve. After allowing the hard bone to encompass the nerve for two years, it was found that the cat used the leg normally, that the nerve conducted impulses through the bone-encircled area, and that, finally, histologic sections showed the presence of axis cylinders in the nerve distal to its point of emergence from the bony canal.

Clinically, it will be recalled that a sectioned nerve shows a greater area of skin with the loss of sensation to light touch than to pin prick, whereas

a compressed nerve gives the reverse picture (Core,[2] Stopford[9, 10]). However, the sensory changes reported above do not agree with this clinical picture, because when the patient suffered the maximum of nerve compression (Fig. 1) the area of light touch (cotton wisp) anesthesia (T) was the second largest involved; and not the least, in the second place, when compression of the nerve again took place after the first operation, this area was the largest (Fig. 9), and not the smallest.

The curious overlap of sensations (Figs. 3, 4, and 5) following the first operation was not duplicated after the second interference (Figs. 12 to 17). It is possible that this overlap may be of particular interest in the study of cutaneous sensitivity in that it may be diagnostic of nerve compression.

CONCLUSIONS

This report proposes to make two contributions to the understanding of meralgia paresthetica:

(1) The cause of the disease is probably a compression of, and tension on, the lateral femoral cutaneous nerve as it passes under the inguinal ligament, because in the three instances in which neurolysis was performed on this nerve in that location there resulted an immediate and progressively favorable increase in the sensibility of the skin supplied by the nerve.

(2) A cure for the disease may be a modified neurolysis operation, by means of which pressure and tension are taken from the nerve, which is then relocated in a slot in the ilium.

In two severe cases, one of which is reported in detail here, the patients were entirely relieved of their symptoms, and had normal sensation restored in the skin. The first patient has been well now over four years, and the second was well when examined two years after the second operation.

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EXTRASKELETAL OSSIFYING TUMORS

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MESOBLASTIC TUMORS containing bone occur which have no connection with the skeleton. In all probability many more such tumors have been reported than have been revealed in this search of the literature because of failure of the authors to indicate the presence of bone in the title of the article.

The presence of calcification and ossification in old hematomata is not an unusual pathologic finding. Other examples of heterotopic bone, not infrequently seen, are ossification in the arteries, heart valves, pericardium and in old tuberculous foci. There are numerous instances of heterotopic bone formation in old abdominal cicatrices. Myositis ossificans is usually continuous with the skeletal system though there may be no connection, as when it involves muscles of the abdominal wall after celiotomy.

In addition to the heterotopic bone formations mentioned above, ossification may occur in neoplasms having no skeletal connection. When the tumor is epithelial in origin, as in the case of carcinoma of the breast, the bone is heteroplastic in nature, coming from the connective tissue.

Ossification of intracranial neoplasms, not arising from the skull, has been observed many times. Alpers[1] reports an osteochondroma arising from the dura and cites two cases by other authors of similar tumors. He also cites four intracranial chondromata not related to the skull.

Sperling and Alpers[33] report an osteolipoma of the brain and record 12 other cases of this type from the literature.

Examples of benign bone tumors in the soft parts in areas other than the brain are also found. An osteoma of the tongue was reported by Magnien and Perrot,[24] and an osteoma of the breast by Roffo and Meabe.[28] Recently, a perirenal retroperitoneal osteoma was reported by Kretschmer.[21]

Jacobson[18] reported two instances of ossifying tumors of the soft parts which, histologically, resembled benign giant cell tumors of bone. In one case, the tumor developed in the thigh, while in the other instance it was found in the popliteal space. Neither tumor was considered malignant clinically or histologically.

The author agrees with Jacobson in believing that since by metaplasia the connective tissue cell may form bone, then it is natural to assume that all types of bone tumors might occur in the soft parts.

Recently, two osteogenic sarcomata, experimentally produced in the soft parts of rats, were reported by Dunning, Curtis and Bullock.[11] These workers injected 1–2 benzopyrine subcutaneously into a group of 842 rats. Various types of tumors resulted. The two osteogenic sarcomata resembled malignant

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primary bone tumors although they developed in the soft tissues. Brunschwig and Roome[5] report having produced a spindle cell sarcoma in the left suprarenal gland of a rat by the implantation of crystals of methylcholanthrine into this organ. Sections revealed scattered small areas showing ossification of the intramembranous type.

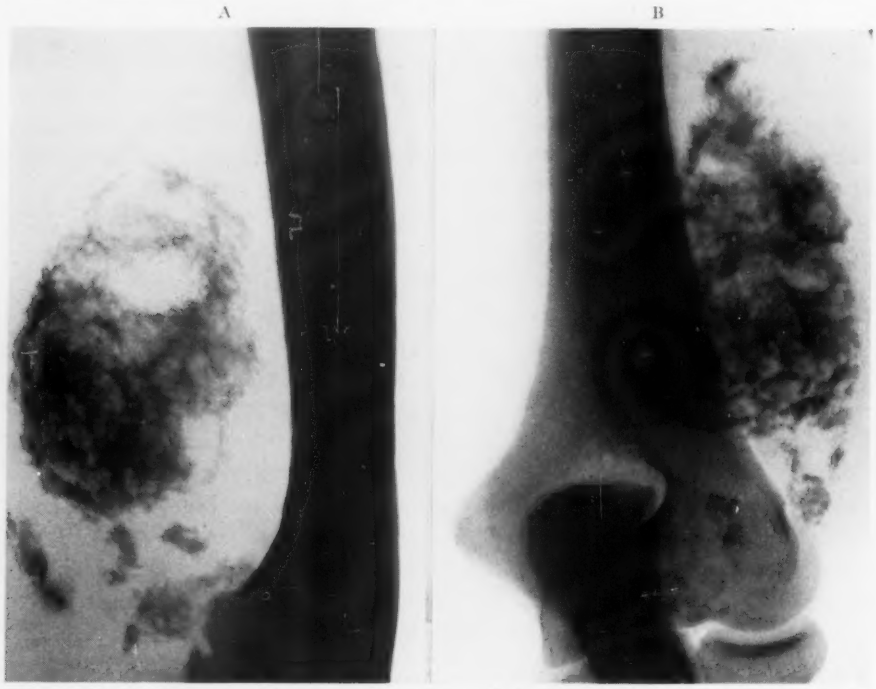


FIG. 1.—Case 1: A and B. Roentgenograms of supracubital region showing extraskeletal oval tumor containing irregular areas of bony density.

Thirty cases of bone-forming malignant tumors in the soft parts were reviewed from the literature (Table I). The histologic report given in most of these cases was compatible with that of a true osteogenic sarcoma. Not all of this group were studied roentgenologically. These tumors occurred at various sites in the body—in the extremities, abdominal wall and viscera, breast and thyroid.

The present study consists of ten cases of extraskeletal ossifying tumors collected from the departments of surgery and pathology of the University of Chicago and from the Bone Sarcoma Registry of the American College of Surgeons.

CASE REPORTS

Case 1.—Bone Sarcoma Registry No. 2033: Case of Dr. T. R. Ross. J. C., male, age 35.

History and Physical.—C. C.: Tumor of arm just above elbow. P. I.: Patient struck left elbow against an object in December, 1936. The pain and swelling following the injury were somewhat relieved by hot dressings.

Roentgenologic examination March 3, 1937, revealed a large oval-shaped mass above the cubital fossa. Scattered throughout the mass were areas of bony density (Fig. 1 A and B). *Roentgenologic Diagnosis:* Calcified hematoma.

TABLE I

SYNOPSIS OF 30 CASES OF BONE-FORMING MALIGNANT TUMORS IN THE SOFT TISSUES

(From the Literature)

Author	Patient and Complaint	Essential Characteristics of Lesion
1. Arnold[2]	Woman, age 67. Goose-egg-size tumor of nipple for 6 mos.	Spindle and giant cells. Islands of cartilage and of osteoid tissue. No mention of metastases. No follow-up after operation. Diagnosis: Osteochondrosarcoma of breast.
2. Bianchi[3]	Woman, age 60. Tumor in right quadrant of abdomen. No jaundice.	At operation, a malignant tumor of gallbladder was removed. Gallbladder contained stones. Tumor arising from fundus showed spindle cells and osteoid tissue and calcification. Numerous mitotic figures. Diagnosis: Osteogenic sarcoma of gallbladder.
3. Broders and Pemberton[4]	Woman, age 71. Growth in right side of neck for 4 mos.	Biopsy. Pleomorphic and spindle cells. Areas of osteoid and tumor bone present. Radium needles inserted. Patient eventually died of sarcoma. Diagnosis: Osteogenic sarcoma of thyroid.
4. Budd and Breslin[6]	Woman, age 59. Lump in chest wall above breast for 28 yrs. Rapid growth for past year.	No x-ray. Hard tumor calcified in some areas. Microscopic: Some areas showed carcinoma cells with alveolar structure. Other areas contained spindle cells, osteoid tissue and bone. One type of tissue merged with the other. Numerous mitotic figures. Diagnosis: Carcino-osteogenic sarcoma of chest wall.
5. Busser[7]	Woman, age 50. Radical mastectomy. Recurrence 2 yrs. later.	Microscopic at first operation showed adenofibroma with some osteoblasts and chondroblasts at the periphery. Recurrence of nodule in scar 2 yrs. later. Immature cells, rapidly growing. Chondroblasts and osteoblasts. Osteoid tissue. Definitely malignant. Diagnosis: Osteochondrosarcoma of breast.
6. Butler and Woolley[8]	Woman, age 68. Tumor, left thigh; 11 yrs. before bruised leg at this site and some swelling had persisted.	X-ray: Soft tissue mass 9x5 cm. Periphery of mass showed areas of irregular calcification suggestive of an "old calcified hematoma." Tumor excised 20x12x10 cm. Microscopic: Round and spindle cells, mitotic figures, some calcium and some true bone. Chest metastases present by x-ray. Died 2 yrs. after onset. No autopsy. Diagnosis: Osteogenic sarcoma arising from calcified hematoma.
7. Caën[9]	Woman, age 59. "Tumor of breast, size of child's head."	Hyalin cartilage and bone present. Diagnosis: Osteochondrosarcoma.
8. Chavannaz and Pierre-Nadal[10]	Woman, age 74. Tumor of thyroid present several years; rapid growth for 2 mos.	Tumor composed of spindle cells, cartilage and bone. Diagnosis: Osteogenic sarcoma of thyroid.
9. Ferrero[12]	Woman, age 29. Tumor of abdominal wall for 2 mos.	Tumor size of "hen's" egg, excised from lower abdominal wall. Recurred and radical excision performed. Microscopic: Very cellular—round, oval and spindle cells. Interlacing trabeculae of bone and osteoid tissue. Diagnosis: Sarcoma.
10. Foerster[13]	Woman, age 60. Tumor of thyroid. Duration not given.	Spindle cells; bone present in tumor. No metastases. Diagnosis: Osteogenic sarcoma of thyroid.
11. Funkenstein[14]	Tumor of thyroid.	Spindle cells. Bone present. No metastases. Diagnosis: Osteogenic sarcoma.
12. Funkenstein[14]		Similar to above case.
13. Gomori[15]	Woman, age 64. Painless lump in right breast for 6 mos. Size of "baby's head"; ulceration.	Simple mastectomy and resection of axillary nodes. Spindle cells, giant cells, mitotic figures, bony trabeculae present. Diagnosis: Osteochondrosarcoma of breast.
14. Haining and Poole[17]	Man, age 76. Hematuria; mass in left kidney region.	Autopsy: Tumor of left kidney which, histologically, was said to be identical with osteogenic sarcoma. Spindle, round and giant cells present. Osteoid tissue and bone. Widespread metastases. Some metastases contained bone.
15. Jaidka[19]	Boy, age 14. Pain and stiffness in right thigh for 6 wks. Tumor in vastus externus.	Hip joint disarticulation. Malignant tumor of fibrous tissue origin present producing bone. Diagnosis: Ossifying sarcoma of vastus externus muscle.

TABLE I (*Continued*)

Author	Patient and Complaint	Essential Characteristics of Lesion
16. Kreibig[20]	Woman, age 50. "Walnut size tumor of breast."	Giant cells, cartilage, osteoid tissue and bone. Diagnosis: Osteosarcocarcinoma of breast.
17. Kubo[22]	Man, age 30. Tumor right side of abdomen.	G. I. x-ray only. Explored: Tumor "size of head" adherent to bowel and peritoneum. Lymph node biopsy showed fibrosarcoma. Autopsy (55 days later): Osteofibrosarcoma of mesentery. Large areas of bone. Some myxomatous tissue.
18. Kurosu[23]	Woman, age 60. "Head-sized tumor" of breast; duration not given.	Died soon after excision. Diagnosis: Osteochondro-angiosarcoma. No autopsy.
19. Mallory[25]	Woman, age 55. Breast tumor; for 3 mos.	Excised. No recurrence in 1 yr. Spindle cells, tumor giant cells. Osteoid tissue, some calcification. Believed to be a sarcoma.
20. Mallory[25]	Woman, age 65. Tumor left thigh; for 2 yrs.	Tumor excised. Recurred. Microscopic: Composed of spindle cells. Tumor giant cells present. Bone trabeculae. Frankly neoplastic process. Bone probably heterotopic, possibly neoplastic. Diagnosis: Sarcoma of thigh containing bone.
21. Pick[26]	Woman, age 51. Tumor of neck, present for several years. Developed tumor of palate and died soon after.	Tumor of neck was sarcoma in thyroid. Mass made up of spindle cells. Bone present in many areas. Widespread metastases. Lung metastases contained bone. No autopsy.
22. Rhoads and Blumgart[27]	Woman, age 21. Lump in right thigh, for 5 wks.	Encapsulated tumor not connected with thigh. Microscopic: Spindle cells, mitoses, osteoid changing into bone. Well 10 yrs. later. Diagnosis: Osteoblastoma.
23. Rhoads and Blumgart[27]	Male, age 37. Swelling in left groin, for 15 mos.	Left inner thigh firm, rounded mass 2x6 cm. X-ray: Calcium density in region of tumor. Microscopic: Immature fibroblasts, many mitoses, new bone, osteoid tissue and cartilage. Well 7 yrs. after excision. Diagnosis: Osteoblastoma.
24. Sailer[29]	Woman, age 59. Lump in right breast, for 6 wks.	Tumor present 4x3 cm. Microscopic: Spindle round cells. Many mitoses. Spicules of bone surrounded by osteoblasts. Osteoid and cartilage present. Well 2 yrs. later. Diagnosis: Sarcoma of breast (osteogenic).
25. Sehrt[31]	Woman, age 44. "Fist-sized" tumor of breast, for 6 mos.	Excised. Microscopic: Giant cells, cartilage, osteoid and bone present. Appearance of bone varied considerably in various areas of tumor. No mention of metastases. No follow-up. Diagnosis: Osteosarcoma of breast.
26. Stilling[34]	Woman, age 53. Large breast tumor. Duration not given.	Osteoid tissue, cartilage and bone in tumor. Metastases to lungs. Diagnosis: Osteosarcoma of breast.
27. Stilling[34]	Woman, age 59. Tumor of breast.	Osteoid tissue and cartilage, spindle and giant cells. Local recurrence 5 wks. after excision. Metastases to distant foci. Diagnosis: Osteosarcoma of breast.
28. Solaro[32]	Male, age 46. Tumor of thyroid region, for 8 mos.	Spindle cell sarcoma of thyroid contained much bone and cartilage. Bony tissue appeared to be rather normally formed. Recurred 2 mos. after operation. Diagnosis: Sarcoma of thyroid (osteogenic).
29. von Hacker[35]	Woman, age 50. Small tumor of left breast, for 20 yrs. Rapid growth for 1 mo.	Cartilage, bone, fibrous tissue and osteoid tissue. Believed to be carcinoma containing bone.
30. Williams[36]	Woman, age 53. Tumor in calf muscles, for 10 mos.	Hard tumor in gastrocnemius. X-ray: Irregular shadow of calcium density. Partially encapsulated at operation. Arose from fascial plane between gastrocnemius and soleus. Diagnosis: Round cell sarcoma forming new bone.

Operation was performed March 15, 1937, and an irregular mass, 8 cm. in diameter, was removed.

On July 29, 1937, a recurrence of the tumor, 4 cm. in diameter, was excised and on October 27, 1937, because of a second recurrence, a shoulder disarticulation was performed.

Pathologic Examination.—Gross: Tissue from first operation. The tissue varies in consistency. Portions of tumor are fibrous and myxomatous, while other areas resemble cartilage. Some areas are calcified.

Microscopic.—The tumor in some areas is quite cellular. The cells are small and have spindle-shaped nuclei. Occasional mitotic figures are seen. Small fat cells are also

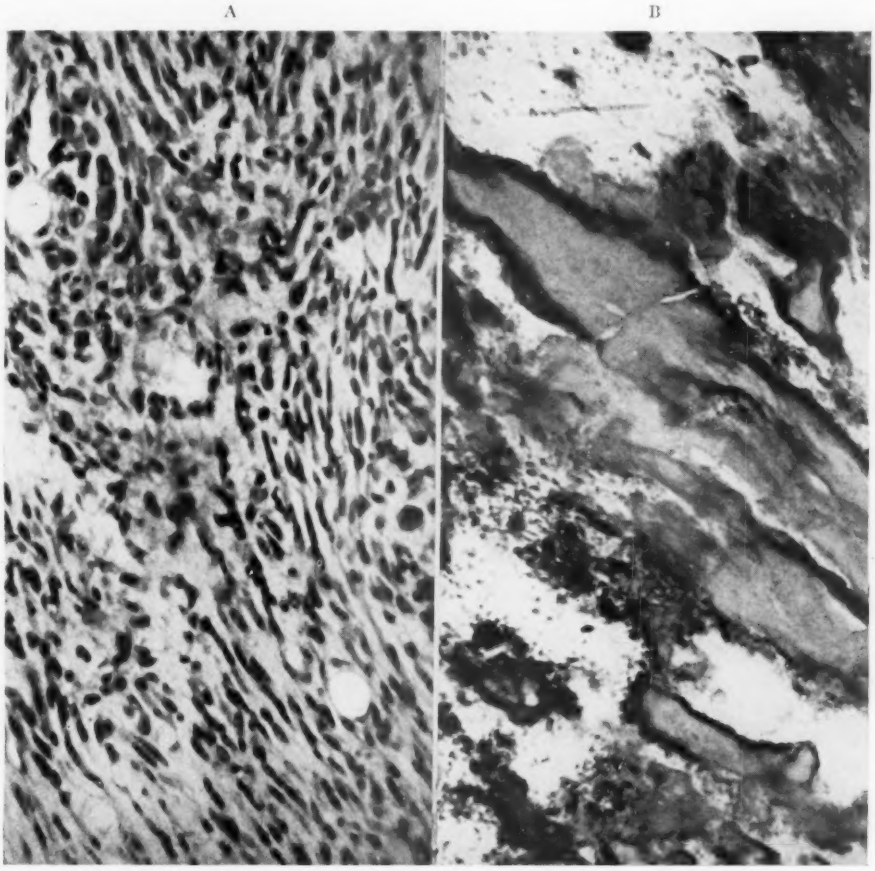


FIG. 2.—Case 1: Microscopic appearance of the tumor. (A) Soft portion. (B) Calcified and ossified portion.

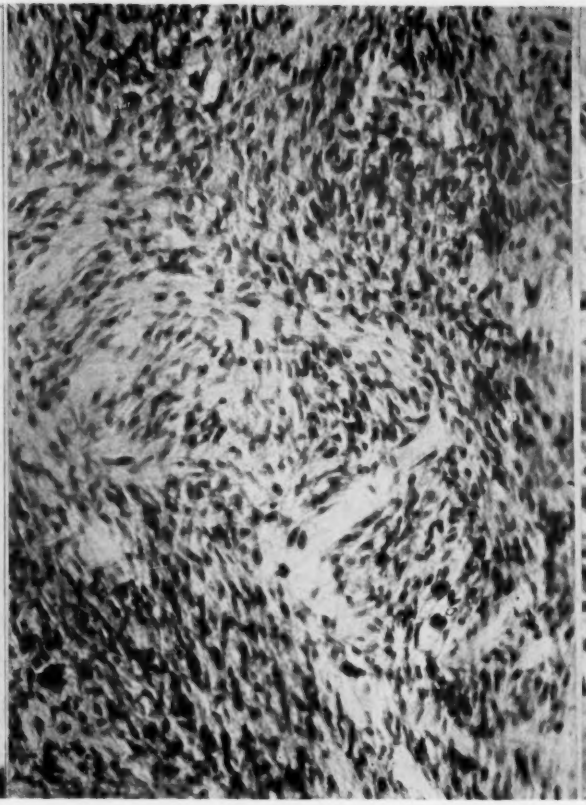
present (Fig. 2 A). In other portions of the tumor large irregular areas of calcification are present and immature cartilage cells are seen. Ossification is occurring in some areas; however, it is difficult to determine from the histologic appearance whether this represents heteroplastic or neoplastic bone formation (Fig. 2 B).

Tissue from the first and second recurrences of tumor show invasion of surrounding muscles. Microscopic examination of the tumor recurrences reveals closely packed cells varying considerably in form and showing more evidence of malignancy as judged by the frequency of mitotic figures and the invasion of muscle. *Pathologic Diagnosis:* Osteogenic sarcoma, extraskeletal.

Case 2.—Bone Sarcoma Registry No. 1396: Registered by Dr. B. L. Coley. S. M., female, age 61, admitted to Memorial Hospital, N. Y., September 8, 1931.

FIG. 3.—Case 2: Roentgenogram of extraskeletal tumor of bony density in mesial aspect of thigh.

A



B

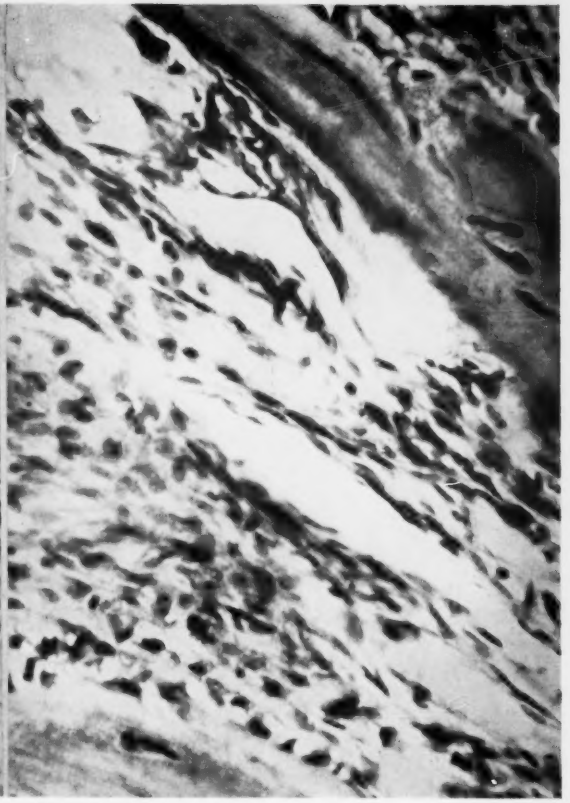


FIG. 4.—Case 2: Microscopic appearance of the tumor. (A) Unossified portion. (B) Ossified portion.

History and Physical.—C. C.: Tumor of left thigh. Ten years previously a slow growing tumor first appeared on the lower inner aspect of the left thigh. Excision was done one year after tumor was first noted.

Subsequent Course.—Two and one-half years before hospital admission a rapidly growing recurrent tumor developed, which was the size of a grapefruit when patient was examined.

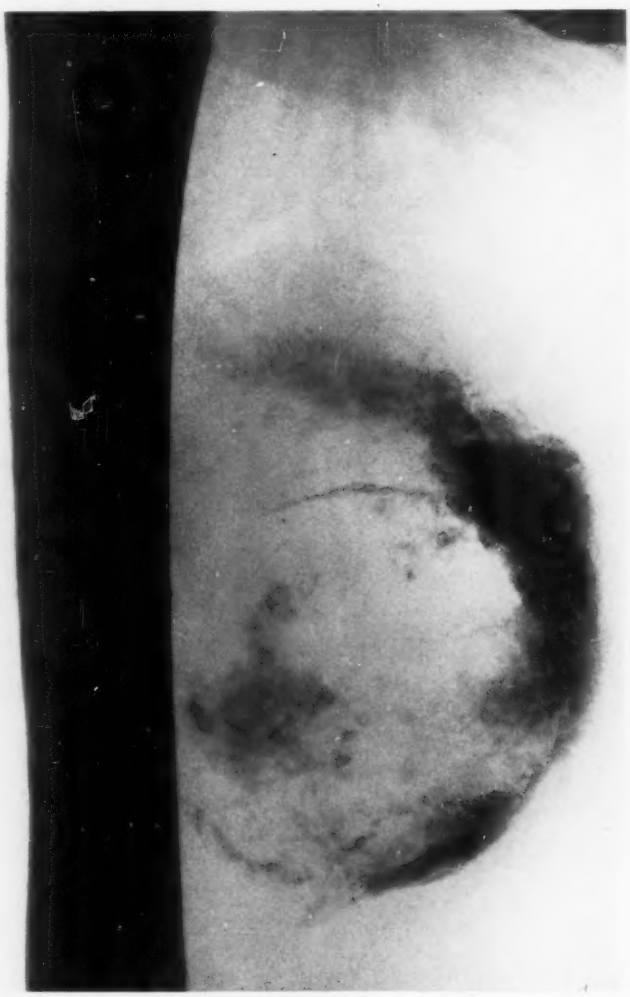


FIG. 5.—Case 3: Roentgenogram of extraskeletal tumor of mesial side of thigh casting shadow of calcium density in its peripheral portion.

Roentgenologic examination showed a large mass of bony density in the lower inner aspect of the left thigh. There was slight radiation at the periphery of the dense shadow.

The tumor was excised July 18, 1931, and diagnosed osteogenic sarcoma. The wound never healed properly. Roentgenotherapy was given and, on February 20, 1932, the leg was amputated. Death occurred two days later.

Microscopic Examination.—The tumor consists mainly of spindle cells growing in whorls and in irregular clumps. Some large giant cells are present. Many cells are

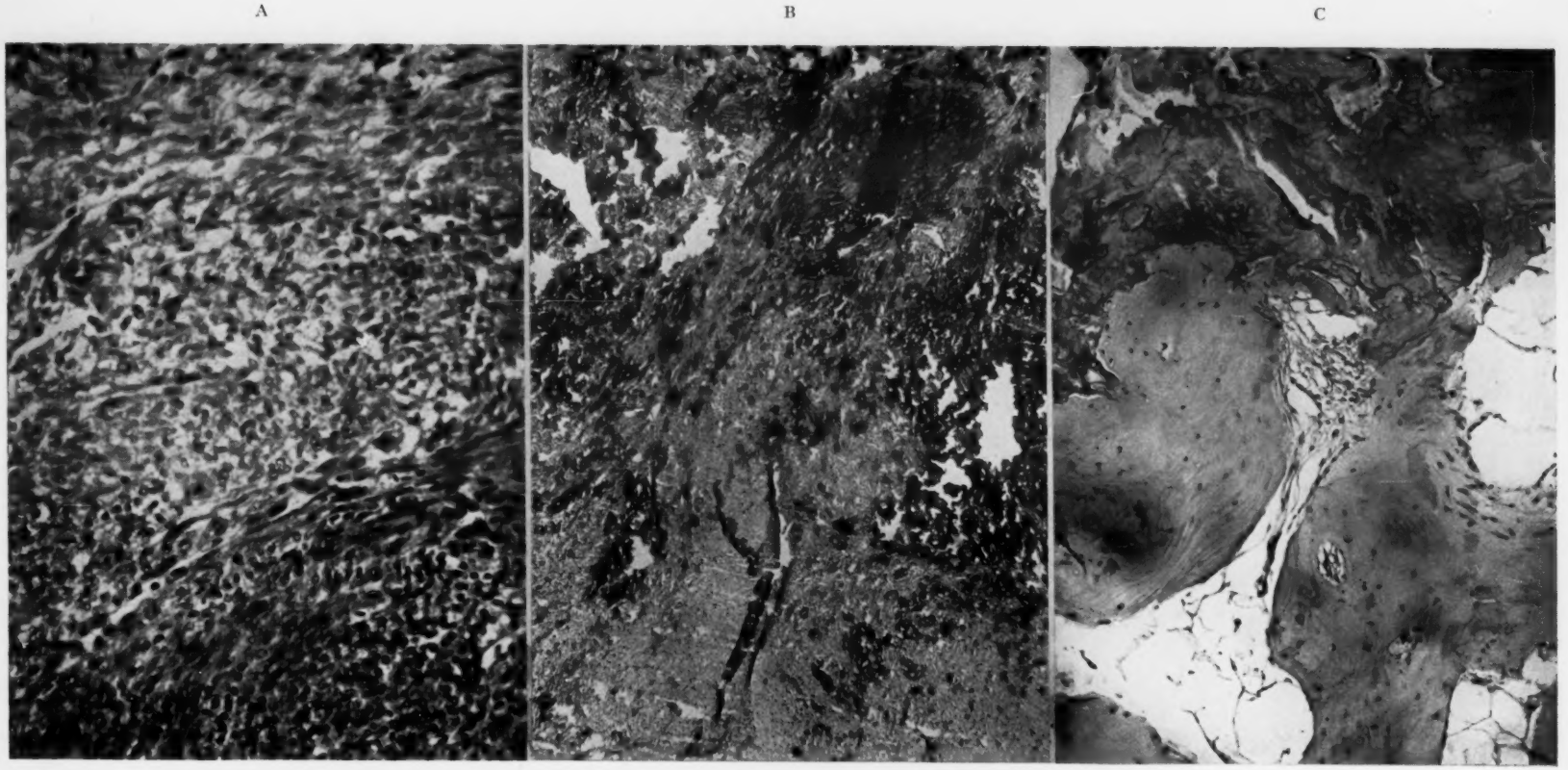


FIG. 6.—Case 3: Microscopic appearance of the tumor. (A) Soft portion. (B) Calcified portion. (C) Calcified and ossified portion.

undergoing mitotic division. There are irregular trabeculae of neoplastic osteoid tissue scattered about the section and small islands of atypically appearing bone. *Pathologic Diagnosis:* Osteogenic sarcoma, extraskeletal.

Case 3.—Bone Sarcoma Registry No. 2051: Case of Dr. Alexander Brunschwig. N. G., female, age 25.

History and Physical.—Swelling in left thigh of nine months' duration. Examination showed an enlargement extending from the buttock to the middle third of the thigh involving chiefly its posterior mesial aspect.

Roentgenologic examination revealed a soft tissue swelling which contained areas of bony density (Fig. 5).

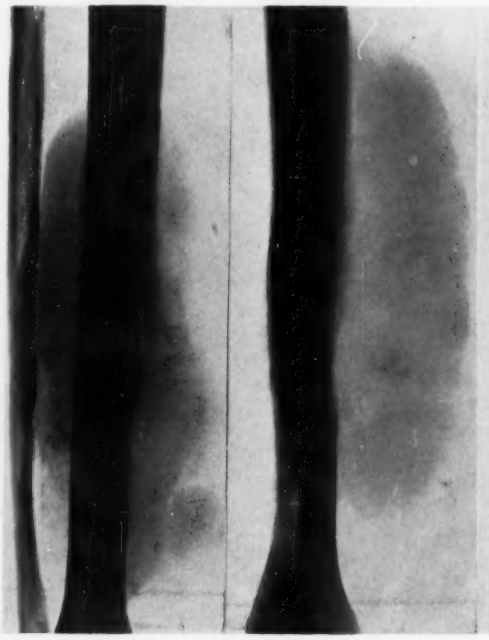


FIG. 7.—Case 4: Roentgenograms showing islands of bony density in extraskeletal tumor.

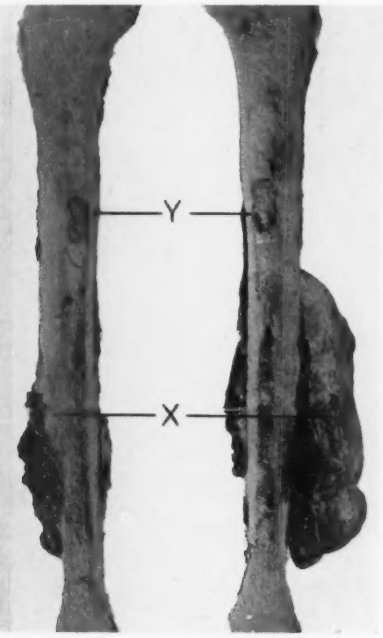


FIG. 8.—Case 4: Extraskeletal sarcoma of soft tissue of leg with secondary erosion of tibia and invasion of (X), and metastasis in (Y) medulla.

Biopsy was performed May 30, 1936, following which 8,000 r units of roentgenotherapy were administered. A second biopsy was taken after the roentgenotherapy.

Pathologic Examination.—Microscopic: Sections of tissue removed on both occasions reveal a preponderance of spindle cells arranged in whorls and bundles. Mitotic figures are present. There are irregular areas of calcification and in some of these areas bone has formed (Fig. 6). *Pathologic Diagnosis:* Fibrosarcoma with degeneration, calcification and heteroplastic bone formation.

Case 4.—Case of Dr. Dean Lewis: M. E. P., male, age 34, admitted to Presbyterian Hospital, Chicago, May 30, 1916.

History and Physical.—C. C.: Tumor of left leg. A hard nodule appeared above the external malleolus 12 years before admission; however, during the 18 months prior to admission growth of the tumor was much more rapid. Examination revealed a mass 17x7x4 cm. on the anterior surface of the left leg (Fig. 7). Amputation was performed above the knee.

Pathologic Examination.—Gross: The tumor is irregular in contour and can be easily lifted away from the tibia, suggesting that it arose outside the bone (Fig. 8).

Microscopic.—The tumor in some areas is quite cellular and in others contains a large amount of collagen. The majority of the cells are oval or rounded in shape and mitotic figures are numerous. Many giant cells are present. Throughout the tumor are small areas exhibiting calcification and ossification. *Pathologic Diagnosis:* Extraskeletal sarcoma with bone formation. The patient subsequently died of metastases.

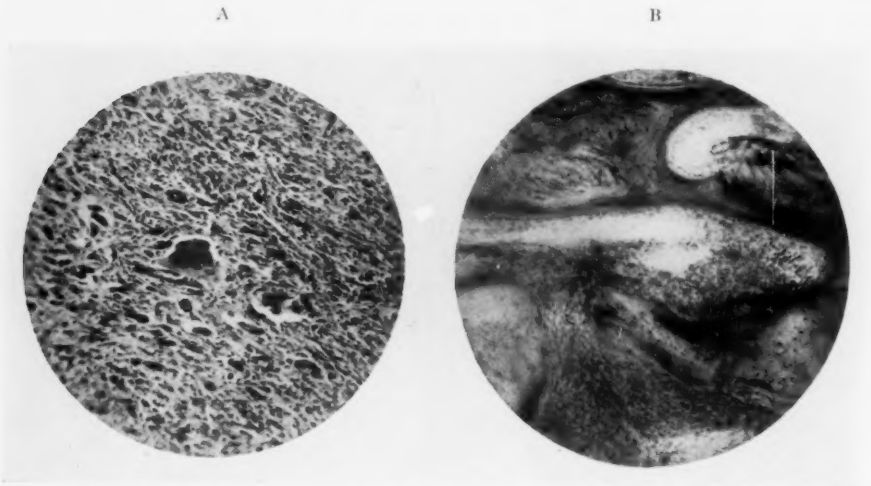


FIG. 9.—Case 4: Microscopic appearance of the tumor. (A) Unossified portion. (×170) (B) Ossified portion. (×110)

Case 5.—Bone Sarcoma Registry No. 1494: Registered by Dr. B. L. Coley. R. M., male, age 19.

History and Physical.—Patient entered Memorial Hospital, New York, September 9, 1932, because of swelling of the face, neck and right arm and right leg of four days' duration.

Roentgenologic examination revealed a large oval shadow of bony density in the left mediastinum and adjacent lung field. The edges of this were somewhat irregular (Fig. 10). Death occurred November 12, 1932.

Necropsy revealed a large tumor in the mediastinum about the base of the heart. It consisted chiefly of dense bone but showed some areas of cartilage. Metastases were found in the brain, pancreas, kidney and lungs.

Microscopic Examination.—The tumor contains interlacing bundles of wildly growing spindle cells. In some areas there are sheets of irregular neoplastic osteoid tissue. Very atypical new bone is found associated with the osteoid tissue (Fig. 11). *Pathologic Diagnosis:* Osteogenic sarcoma, extraskeletal.

Case 6.—Bone Sarcoma Registry No. 2131: Case of Dr. Philip Lewin. M. S., female, age 28.

History and Physical.—Pain in left gluteal region began in December, 1936, and one month later swelling was also noted in this area. In October, 1937, a longitudinal fusiform mass, 6 cm. in its greatest diameter, was present in the gluteal region. A roentgenogram revealed a soft tissue mass with blotchy areas of increased density showing calcification (Fig. 12).

The mass was excised by Doctor Lewin October 19, 1937, at the Michael Reese Hospital, Chicago. The greater portion of the tumor was soft, in some areas having a

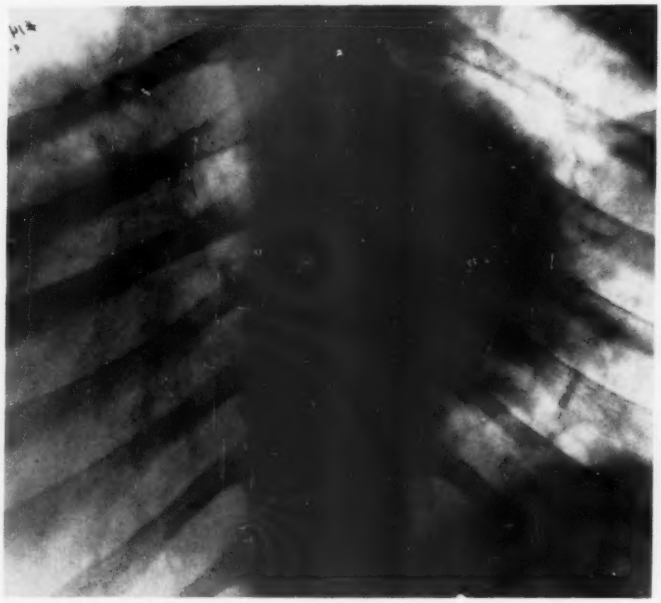


FIG. 10.—Case 5: Roentgenogram showing the sarcoma casting an oval shadow of bony density in the left mediastinum.

A B

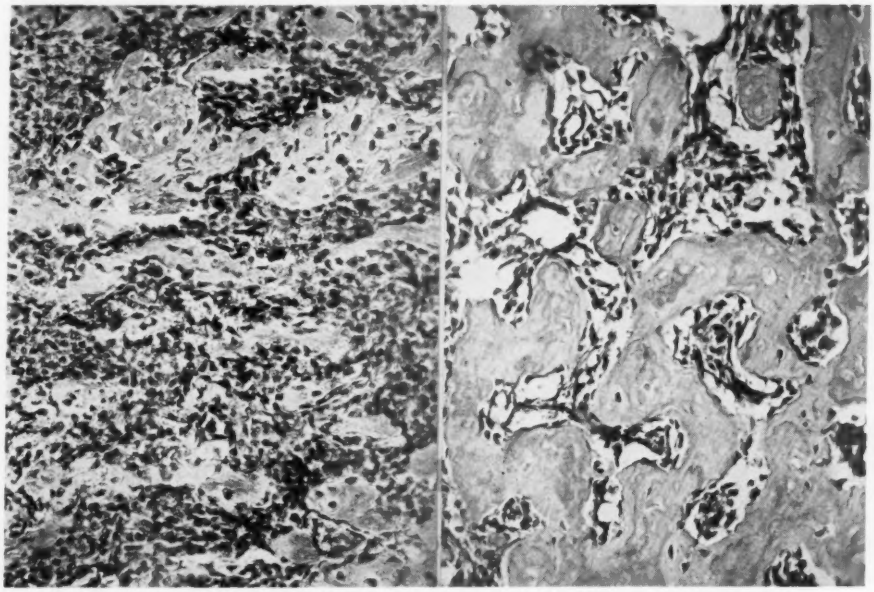


FIG. 11.—Case 5: Microscopic appearance of the tumor showing (A) Round and spindle cells and osteoid tissue. (B) Trabeculated bone.

FIG. 12.—Case 6: Roentgenogram showing the chondrosarcoma of gluteal region with blotchy areas of calcium density.

A B

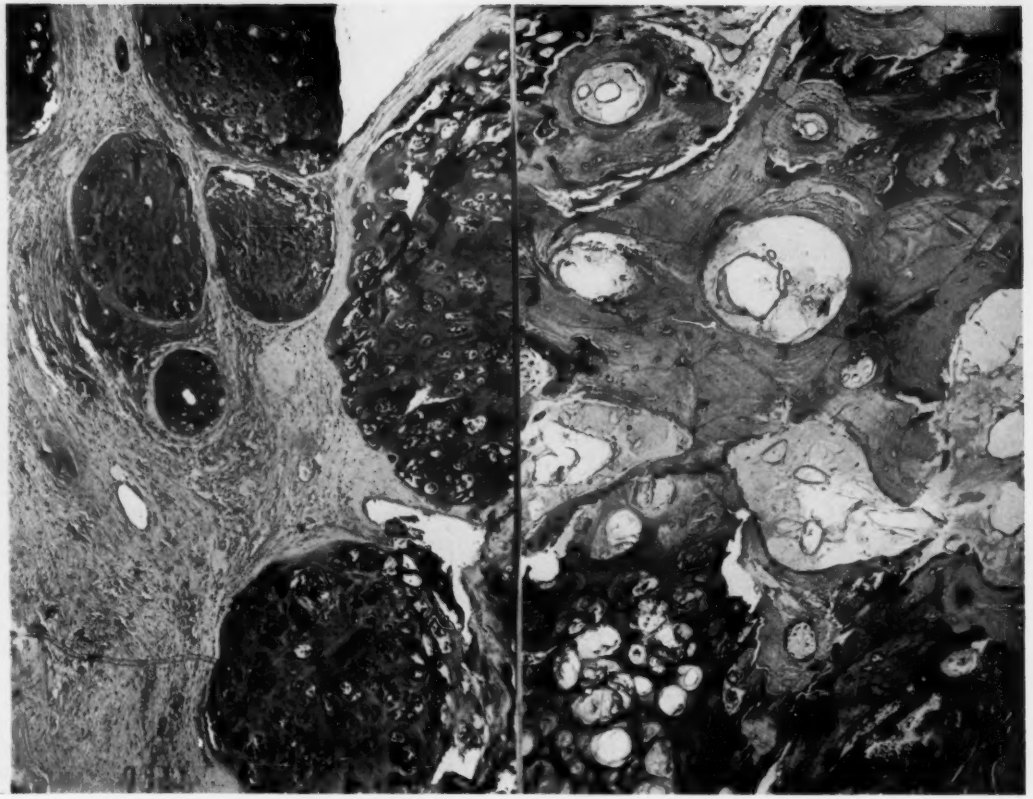


FIG. 13.—Case 6: Microscopic appearance of the tumor showing (A) Cartilaginous nodules about periphery. (B) Ossified and calcified portion.

gelatinous character, while in other areas its consistency was that of bone. Over a small area the tumor was in contact with the ilium. Roentgenotherapy was given after the operation.

Pathologic Examination.—Microscopic: Sections reveal a rather varied appearance. The tumor is composed mainly of cartilage and the large cartilaginous islands are surrounded by dense fibrous tissue. The cartilage cells vary greatly in size and arrangement. Calcification is present in some areas and bone formation is also seen (Fig. 13 A and B). Large myxomatous areas are present which merge into masses of immature cartilage cells. *Pathologic Diagnosis:* Chondrosarcoma, extraskeletal.

On April 16, 1939, a roentgenogram revealed a recurrent mass, calcification being noted in this mass also. Operation was refused.

Case 7.—Bone Sarcoma Registry No. 2055: Case of Dr. C. Howard Hatcher. P. P., male, age 29, entered the University of Chicago Clinics, August 7, 1936.

History and Physical.—Eighteen months before admission pain was noticed in the right hip. This increased greatly in severity and radiated down the leg. Examination revealed a mass, 4x4 cm., in the region of the greater trochanter. Tenderness was also noted in this area. Roentgenograms revealed a soft tissue mass containing areas of bony density in the region of the right hip. There was no connection between the increased density of the tumor and the pelvis (Fig. 14).

On August 12, 1936, a mass, 10x10x8 cm., was excised from an area which involved the deep fascia overlying the gluteus medius midway between the greater trochanter and the ilium. Grossly, the tumor was made up of firm fibrous tissue containing some calcified areas.

Pathologic Examination.—Microscopic: Section reveals large areas of closely packed fibrous tissue cells. The fibrous tissue cells are growing in interlacing strands and bundles. Throughout the fibrous tissue are numerous clumps of deeper staining cells with round or oval nuclei having a rather indefinite cytoplasmic outline. Numerous mitotic figures are seen. In a few areas these cells form papillary-like structures suggestive of epithelial origin. Some small areas of calcification are undergoing ossification. There are also some large mature bone islands, the bone apparently having been formed by the intramembranous method. Muscle invasion by the tumor is seen in some areas (Fig. 15 A and B). *Pathologic Diagnosis:* Bursal sarcoma with ossification in primary tumor.

Subsequent Course.—Roentgenotherapy was given after operation and following this the patient was lost sight of until September, 1937. At this time he complained of more pain, hemoptysis and loss of weight. Roentgenograms showed metastatic lesions in the chest and osteoclastic lesions in the left ilium, left femur and before death occurred on January 28, 1938, lesions were also demonstrated in the lumbar spine (Fig. 16).

Autopsy.—Dr. N. B. Friedman: Revealed metastasis to the right peri-iliac and peri-aortic nodes, right iliopsoas muscle, right ureter, urinary bladder, kidneys, thyroid, liver, heart, spleen, lungs and bones.

Pathologic Examination.—Microscopic: A large section made through the lumbar vertebrae showed them to be extensively eroded by tumor, and a bony bridge consisting of tumor and bony trabeculae joined the second, third and fourth lumbar vertebrae. The metastatic tumor in other areas showed no evidence of bone formation. *Pathologic Diagnosis:* Sarcoma of gluteal region, possibly of bursal origin, with ossification in the primary tumor.

Case 8.—Case of Dr. Alexander Brunschwig: W. P., male, age 20, entered University of Chicago Clinics, March 3, 1937.

History and Physical.—C. C.: (1) Swelling of left forearm for ten years. (2) Multiple soft tumors over torso and extremities for 11 years. (3) Coffee-colored plaques over torso and extremities for 11 years.

Examination revealed small masses located along the course of peripheral nerves

FIG. 14.—Case 7: Roentgenogram showing the sarcoma of the right gluteal region casting shadows of bony density.

A

B

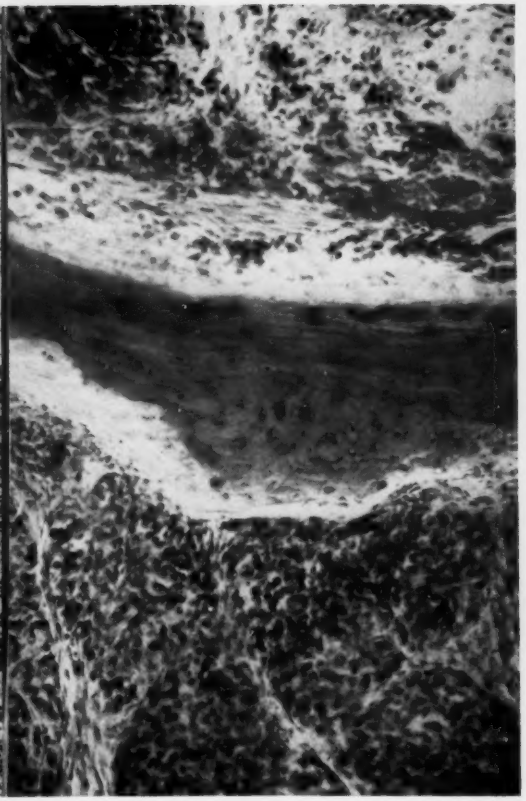


FIG. 15.—Case 7: (A) Microscopic appearance of the gluteal tumor. (×175). (B) Shows ossified and unossified portions of the tumor. (×225)

over the body and extremities. The tumors were larger and more numerous over the distal end of the left forearm. One of these tumors was very hard in consistency. A roentgenogram showed an area of increased density within the soft tissue mass. This density, which was not connected with the skeleton, was interpreted as being ectopic bone (Fig. 17).

On March 4, 1937, through a long elliptical incision, a large mass of neurofibromatous tissue was excised. The mass contained 15 small, whitish, encapsulated tumors surrounded by fat. A piece of bone, 5x2 cm., was present.

FIG. 16.—Case 7: Roentgenogram showing metastasis in the third lumbar vertebra, with a bridge of bony density extending from the second to the fourth lumbar vertebrae.

FIG. 17.—Case 8: Roentgenogram showing an extraskeletal shadow of bony density and deformed ulna in a case of von Recklinghausen's neurofibromatosis.

Pathologic Examination.—Microscopic: The soft tissue is composed of cells having rounded or oval nuclei and rather indistinct cytoplasmic borders. There is a large amount of intercellular material consisting, largely, of fine wavy bundles. No mitotic figures are present (Fig. 18 A). The bone is mature in appearance and the marrow spaces within it contain both fatty and hematopoietic marrow (Fig. 18 B). *Pathologic Diagnosis:* von Recklinghausen's neurofibromatosis with bone formation in a neurofibroma.

Case 9.—Case of Dr. Evarts Graham: An incidental finding in a routine autopsy was a pararenal, bony, oval tumor about 5 cm. in diameter. This retroperitoneal encapsulated mass, consisting of cancellous bone, had no connection with the kidney or the vertebral column.

Pathologic Examination.—Microscopic: Section shows the central portion of the tumor to be made up of dense trabeculated bone, while the periphery is more spongy in appearance. The marrow is fibrous in most areas though there is a small amount of hematopoietic marrow present. There is evidence of proliferation of the bone at the periphery; however, there seems to be no tendency toward rapid growth (Fig. 19).

A

B

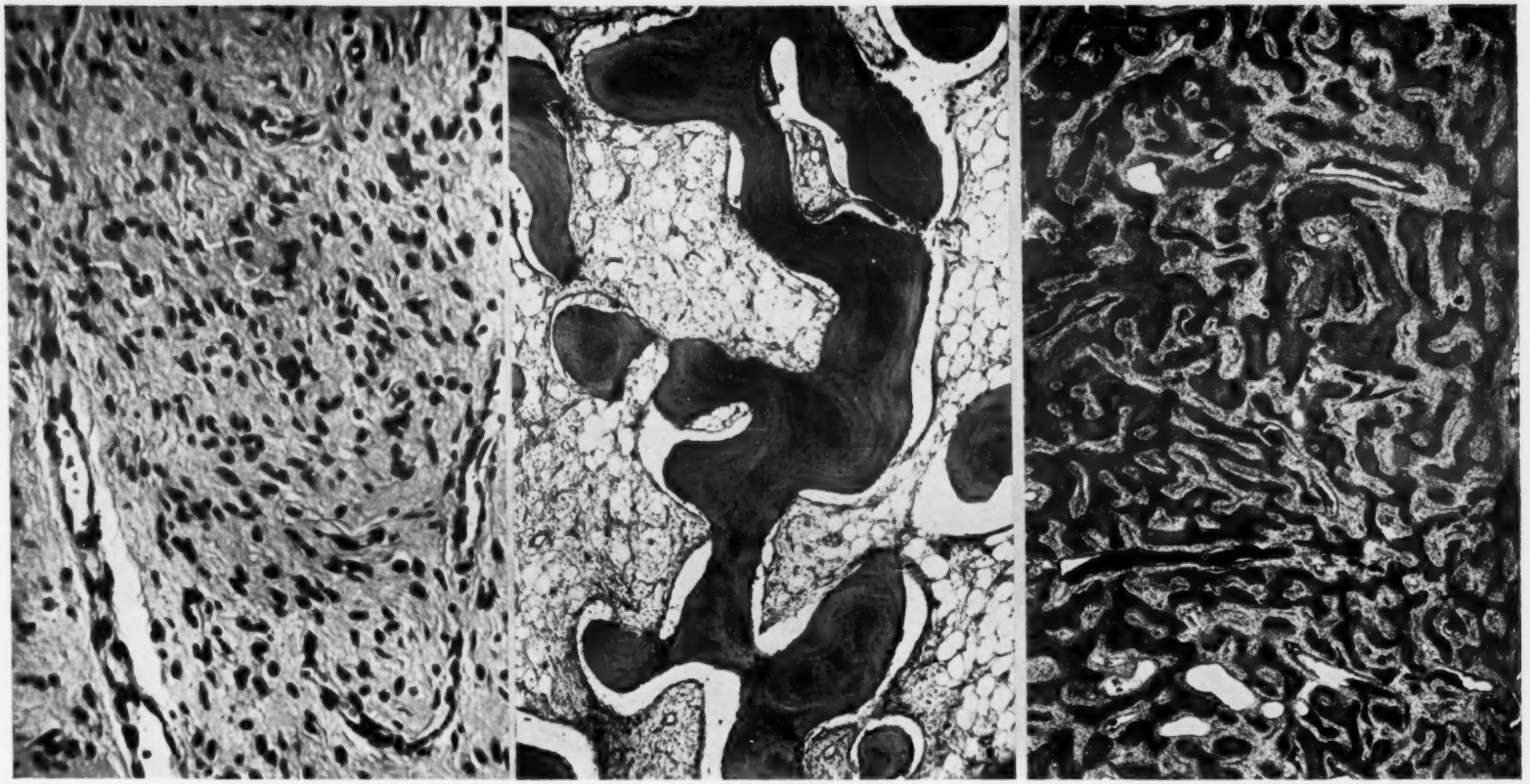


FIG. 18.—Case 8: Microscopic appearance of the tumor. (A) Soft parts. (B) Bone.

FIG. 19.—Case 9: Microscopic appearance of the fibrous osteoma.

This tumor is apparently similar to the case reported by Kretschmer.[21] *Pathologic Diagnosis:* Fibrous osteoma, retroperitoneal.

Case 10.—Case of Dr. Charles Rowan: A young man with a firm tumor was operated upon, December 10, 1911, at Cook County Hospital, Chicago, by Doctor Rowan. Local excision was done. No follow-up of the subsequent course is available.

Pathologic Examination.—Gross: The oval tumor, approximately 10x6 cm. in size, on section consists of firm fibrous tissue and contains scattered areas of bone.

Microscopic.—Section shows the soft portion of the tumor to be composed of fibrous tissue of varying degrees of maturity. A large island of mature bone is present. Its spaces contain both fatty and hematopoietic marrow. At the periphery of one bony spicule is a layer of cartilage which is being invaded by blood vessels and osteoblasts. *Pathologic Diagnosis:* Osteoma of thigh.

SUMMARY AND CONCLUSIONS

(1) Ten cases of extraskeletal ossifying tumors are reported; of these, four are osteogenic sarcomata, one, a fibrosarcoma, with degeneration, calcification and heterotopic bone formation; one, a chondrosarcoma; one, a bursal sarcoma, with ossification in the primary tumor; one, a case of von Recklinghausen's neurofibromatosis, with ossification in a neurofibroma; and two are fibrous osteomata.

(2) This study illustrates the totipotency of neoplastic, mesoblastic tissue.

(3) Myositis ossificans offers the most difficulty in distinguishing heteroplastic from neoplastic bone formation in the soft tissues.

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THE TREATMENT OF STAPHYLOCOCCAL CAVERNOUS SINUS THROMBOPHLEBITIS WITH HEPARIN AND CHEMOTHERAPY

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BACTERIEMIC STAPHYLOCOCCAL CAVERNOUS SINUS THROMBOPHLEBITIS of the anterior or ophthalmic type has been so uniformly fatal that it seems proper to record the survival of two consecutive cases treated with a combination of heparin and chemotherapy. These cases are summarized as follows:

CASE REPORTS

Case 1.—M. G. H. No. 243620: Female, age 31, high school teacher, entered the hospital April 5, 1940, with a nasal furuncle of five days' duration. She had received sulfanilamide at home for three days but the development of signs and symptoms of cavernous sinus thrombophlebitis prompted her physician to refer her to the hospital.

The physical findings on entry are summarized in Table I and the clinical course is shown in Chart 1. Figures 1 and 2 show the patient's appearance on entry and nine weeks later. The clinical course is described further in the following notes:

First hospital day: Heparin and sulfapyridine started.

Fourth hospital day: Sulfathiazol substituted for sulfapyridine.

Eleventh hospital day: Pulmonary infarct.

Seventeenth hospital day: Heparin stopped after a total dosage of 225,000 units.

Twentieth hospital day: Sulfathiazol stopped.

Thirty-fourth hospital day: Clinical signs of meningitis confirmed by lumbar puncture. Sulfapyridine started.

Forty-ninth hospital day: Meningitis still present. Sulfathiazol substituted for sulfapyridine.

Fifty-seventh hospital day: Afebrile and symptomatically improved.

Seventy-seventh hospital day: Discharged home; taking sulfathiazol.

At the time of discharge there was a partial III nerve and complete VI nerve paralysis on the right. Chemotherapy was continued for a total period of four months at which time the spinal fluid protein had returned to normal. The only apparent residuals of the illness are a slight ptosis of the eyelid and high voltage fast brain waves in the electroencephalogram.

Case 2.—M. G. H. No. 80045: Male, age 41, engineer, entered the hospital May 14, 1940, with the diagnosis of acute frontal sinusitis of one week's duration. Physical examination revealed a nasal furuncle and the diagnosis of acute sinusitis was not supported. The clinical course of this patient is summarized in Chart 2 and below:

First hospital day: Sulfapyridine started.

Fourth hospital day: Clinical signs as shown in Table I and Figure 3. Heparin started.

Fifth hospital day: Pulmonary infarct.

Eleventh hospital day: Sulfathiazol substituted for sulfapyridine.

Nineteenth hospital day: Heparin stopped after a total dosage of 580,000 units.

Twenty-eighth hospital day: Appearance as shown in Figure 4 and clinical findings as shown in Table I.

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FIG. 1.—Case 1: Showing patient's appearance at time of admission.

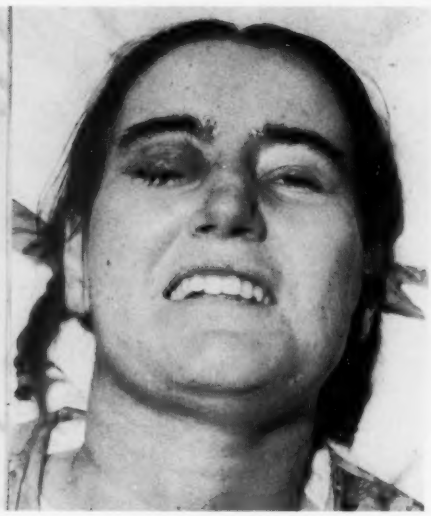

FIG. 2.—Case 1: Showing patient's appearance nine weeks later.

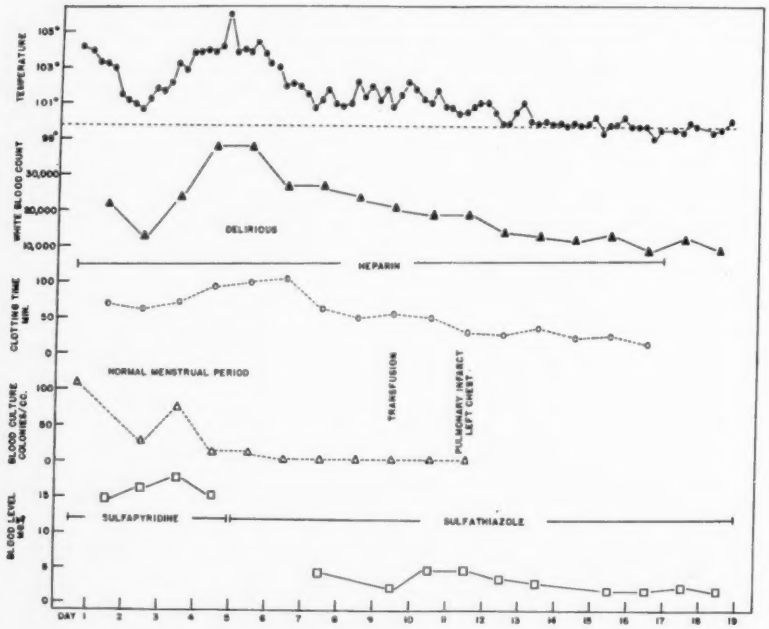

CHART 1.—Case 1: The heparin was obtained from Connaught Laboratories of Toronto. 20,000 units of heparin were added to 1,500 cc. of isotonic saline or glucose solution and administered by constant intravenous drip at a rate sufficient to maintain the clotting time of the blood at about 90 minutes as determined by the five-tube method.

FIG. 3.—Case 2: Showing patient's appearance at time of admission.

FIG. 4.—Case 2: Showing patient's appearance four weeks later.

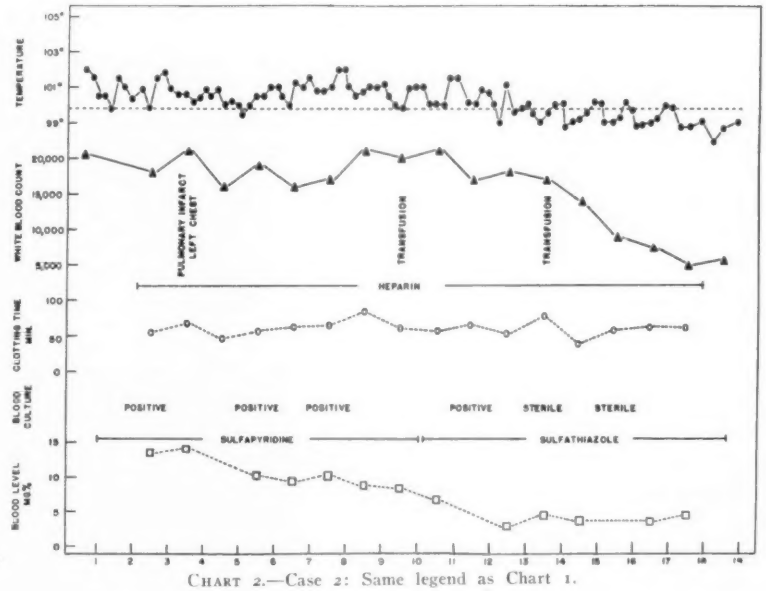

CHART 2.—Case 2: Same legend as Chart 1.

TABLE I

SUMMARY OF CLINICAL FINDINGS

Findings:	Case 1		Case 2	
	On Entry	After Four Weeks	On Entry	After Four Weeks
1. Edema:				
Eyelid	+	0	+	0
Bridge of nose	+	0	+	0
2. Exophthalmos	+	+	+	+
3. Retinal hemorrhages	+	0	0	0
4. Palpable frontal veins	+	0	+	0
5. Diplopia	+	+	+	+
6. Cranial nerve palsies				
III oculomotor	+	0	+	0
ptosis	+	+	+	0
IV	+	0	0	0
V 1st div.	+	0	+	+
3rd div. (motor)	+	0	0	0
VI	+	+	+	0
VII (peripheral)	+	0	0	0
VIII	0	0	0	0
7. Evidence of meningitis	+	+	0	0
8. Staphylococcus blood cultures	+	0	+	0
9. Spinal fluid cultures	0	+	0	0

Sulfathiazol was given for three months, at which time the spinal fluid protein was normal. The patient still has a residual hypesthesia of the left frontal region.

DISCUSSION.—The coincident use of chemotherapy and heparin has led to the survival of two consecutive patients with bacteriemic staphylococcal cavernous sinus thrombophlebitis of the ophthalmic type. These two patients ran almost parallel courses in that:

(1) Both developed pulmonary infarcts while receiving heparin. These infarcts healed uneventfully.

(2) Bacteriemia persisted for several days (eight days and six days, respectively); and ten days of treatment was necessary before clinical improvement was definitely reassuring as to the final outcome.

(3) Both patients developed palpable thrombosis of the frontal veins.

(4) Intracranial infection persisted for many weeks after the external evidence of infection had subsided. This was controlled by chemotherapy alone.

(5) Cranial nerve paralyses, demonstrable at the height of the disease, cleared remarkably well during convalescence.

Sulfapyridine was chosen as the drug with which to start treatment because it was known to diffuse into the spinal fluid more effectively than sulfathiazol. During the first few days of treatment Case 1 developed an increase in temperature and disorientation which suggested drug toxemia. Sulfathiazol was substituted for sulfapyridine with continued clinical improvement. Apparent recovery and omission of chemotherapy in Case 1 was followed by the development of a chronic staphylococcal meningitis which did not respond to sulfapyridine but which did respond to sulfathiazol. Full sulfathiazol dosage sufficient to maintain a blood level of 5 mg. per cent was necessary to control this meningitis. In Case 2 it was felt that prolonged treatment with sulfathiazol would be necessary to control this late chronic meningitis,

and it was again determined that the maintenance blood level had to be about 5 mg. per cent to control the infection. Sulfathiazol in adequate dosage seems to be the drug of choice for the treatment of this type of infection.

The use of heparin is quite naturally suggested by the pathology of cavernous sinus thrombophlebitis but there is another important justification of its use. There is reason to believe that staphylococcal bacteriemia usually arises from foci of septic thrombophlebitis in and around areas of suppuration. Such a conception indicates that the attack upon any staphylococcal bacteriemia should attempt to prevent the extension of septic thrombi as well as to destroy the bacteria. The combination of chemotherapy and heparin in these two cases has given better results than has been observed with chemotherapy alone.

CONCLUSIONS

(1) Two consecutive cases of bacteriemic staphylococcal cavernous sinus thrombophlebitis of the anterior type have been successfully treated by a combination of chemotherapy and heparin.

(2) Sulfathiazol, given in dosages sufficient to maintain a blood level of 5 mg. per cent and continued for a long period after the heparin has been discontinued, seems to be the chemotherapeutic agent of choice.

INTRANASAL GRANULOMA OF THE SPOROTHRIX TYPE PRODUCING MARKED NASAL DEFORMITY

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INTRANASAL lesions of the type illustrated by the following case report are rare. This lesion had caused marked nasal deformity before biopsies were obtained which revealed histopathologic features resembling those of sporotrichosis.*

Case Report.—A female, age 31, an artist who had worked in pottery and painting in New York, Kentucky and Illinois, gave a history of nasal bleeding and discharge for three years when first seen by one of us in 1937. She had been relatively well before 1934. By 1935 a thickening had developed in the midportion of the nose, with a depression near the bony-cartilaginous juncture. The local symptoms persisted and deformity progressed despite much treatment. Numerous laboratory studies failed to demonstrate the cause. In April 1936, the first biopsy from the nasal mucosa was described as follows: "Sections show minute bits of stratified squamous epithelium, mucous membrane, portions of blood clot and small portions of connective tissue. These latter are richly infiltrated by polynuclear leukocytes and lymphocytes. . . . In some portions of the connective tissue there are multinucleated giant cells, but one does not recognize any well-defined tubercles. Plasma cells are fairly numerous . . . (Fig. 1). *Pathologic Diagnosis:* Chronic purulent inflammation, possibly on the basis of an underlying granuloma."

In July 1936, roentgenograms of the sinuses, previously clear, showed "edema and absorption of both ethmoids. Both antra and sphenoids involved. The nose shows a saddle-nose deformity below the nasal bones." Roentgenograms of the lungs were normal.

The nasal deformity was marked when we first saw the patient in 1937 (Fig. 2). The coincident contracture had reduced the right nasal passage to one-third and the left to less than one-third of the normal size, preventing good visualization of the intranasal lesion. However, polypoid tissue, crusts and sticky sanious secretions could be seen, especially marked on the left side. The gums were red-rimmed but not swollen, and granulation tissue-filled pockets lay between some of the teeth. The rest of the physical examination was normal.

A biopsy of the gums disclosed chronic inflammation with many plasma cells and neutrophiles, small abscesses and a few small multinucleated cells. Wassermann and Kahn tests were negative, both before and after the injection of arsenicals. The spinal fluid was normal as were blood counts and urinalyses. A roentgenogram demonstrated the deformity of the nose but no disease of the nasal bones (Fig. 3). Roentgenograms of the thorax and sinuses were interpreted as normal. A large number of tests for allergy were negative. Smears and cultures of nasal secretions revealed staphylococci and streptococci but no acid-fast organisms. Dark-field examinations failed to show spirochetes. Two species of fungi, grown on Sabouraud's medium from nasal secretions, were pronounced nonpathogenic.† Neither culture produced lesions when injected into

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* We are indebted to Dr. C. J. Imperatori, of New York City, Dr. Joseph E. Schaefer, of Chicago, Ill., and Dr. Gordon New, of Rochester, Minn., for these biopsies.

† By Dr. Rhoda Benham of Columbia University.

small laboratory animals.* The patient's serum agglutinated spores of a culture of *Sporotrichum schencki* in dilutions up to 1:320, while a control serum agglutinated the same spore suspension only in dilutions of 1:20 and 1:40.* Cultural studies and animal inoculations were again negative in 1939.† Throughout the period of study, the lesions

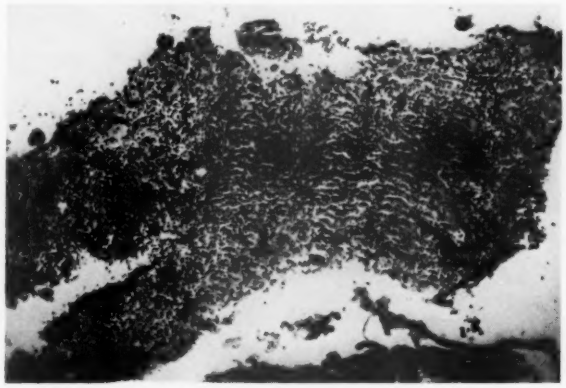

FIG. 1.—First biopsy, April 1936: Section stained with H. and E. (×125). Fragment densely infiltrated with plasma cells and lymphocytes, with a few neutrophiles and, on the left, giant cells.

proved resistant to various types of local and general therapy and general symptoms were negligible save during treatment with iodides to which the patient was hypersensitive. The two biopsies secured in October, 1937 and February, 1939 are described below, and illustrated by Figures 4, 5, 6 and 7.

FIG. 2. FIG. 3.

FIG. 2.—(A). Showing the nasal profile of the patient prior to 1934–1935. (B). Showing the nasal profile of the patient in the summer of 1937.
FIG. 3.—A profile roentgenogram of the nose in the summer of 1937.

* According to Dr. Bertha Kaplan Spector of the University of Chicago.
† At the Mayo Clinic.

Histopathology.—Only the original H. and E. sections of the first biopsy were available, but sections of the others were stained by methods suitable for demonstrating bacteria and other organisms. All three biopsies were similar. The fragments were obviously parts of a polypoid granuloma, covered by stratified squamous epithelium and focally ulcerated. A thin exudate lay over the erosions and a few neutrophiles invaded

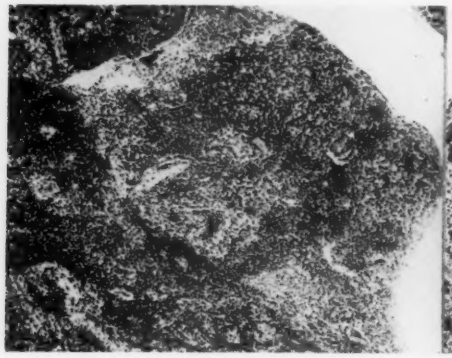

FIG. 4.—Second biopsy, October 1937: Section stained with H. and E. (×125). Polypoid, ulcerated mass densely infiltrated with plasma cells and other leukocytes; giant cells near right border.

FIG. 5.—Second biopsy: Section stained by Unna-Pappenheim method (×125). Loose vascular granulation tissue at surface of polypus, with many plasma cells, a few neutrophiles and several giant cells in deeper portion.

the intact epithelium. The superficial zones of the fragments were edematous and very vascular, infiltrated by plasma cells and lymphocytes. They had focal accumulations of neutrophiles and macrophages many of which contained nuclear débris. A few multinucleated giant cells were present. The denser deep portions had many plasma cells,

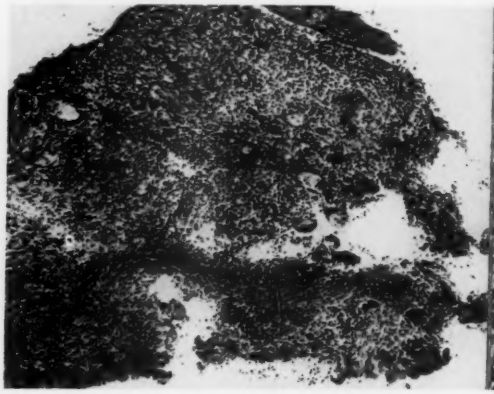

FIG. 6.—Second biopsy: Section stained by Unna-Pappenheim method (×125). Dense granulomatous tissue from deep region with tuberculoid foci and many giant, epithelioid, and plasma cells.

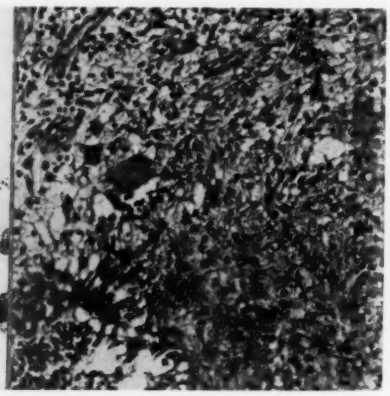

FIG. 7.—Third biopsy, February 1939: Section stained with H. and E. (×275). The "syphiloid, tuberculoid and ecthymatoid"[4] features illustrated by top zone, with many plasma cells and lymphocytes; middle zone, with multinucleated and epithelioid cells; dense lower zone, with focus of neutrophiles bordered by epithelioid cells.

epithelioid and giant cells, and some eosinophiles and mast cells scattered through a fibrous stroma. Neutrophiles were scarce save in small foci which combined the features of miliary tubercles and small abscesses. In these lesions neutrophiles were mixed with seminecrotic tissue in their centers while epithelioid cells formed their borders. While these foci were tuberculoid there were no typical tubercles. The numerous giant cells were scattered irregularly and while some were of the Langhans' type others had grouped nuclei and the bizarre forms of foreign-body giant cells.

Careful search revealed a few gram-positive cocci and rods and gram-negative rods, all on or near the eroded surfaces. Deeper, and usually in macrophages, were a few coarse round or oval gram-positive bodies, the latter 4–5 μ long and 2–3 μ broad. These were blue with H. and E. and Giemsa stains and red with the Unna-Pappenheim stain. While these bodies stained as do gram-positive bacteria or fungi they were coarser than most bacteria. However, they were not positively identifiable as fungus spores.

Discussion of Histopathologic and Clinical Features.—The almost identical granulomatous features of all three biopsies would seem to point to the prolonged action of a single causative agent. Foreign bodies, chemicals, allergens and living organisms all may incite inflammation of a granulomatous character. In consideration of the etiology in this case the action of a foreign body could be excluded. Although this patient was hypersensitive to iodine, this drug probably did not play a part in etiology. The disease was established before iodides were given, and the histopathology was unlike that attributed to iodine.[7] Other chemical and allergic factors could be excluded on the basis of the various tests made. On the whole the most probable cause would seem to be an infection. In view of the slow progression of the nasal lesion and the mild general symptoms, an infectious agent of low pathogenicity would be suspected.

The histopathology was unlike that of the common chronic pyogenic infections, and of the less common granulomata attributed to pyogenic organisms, such as botryomycosis and granuloma pyogenicum. From the clinical, laboratory and morphologic data both syphilis and tuberculosis could be excluded. Rarer granulomata also may affect the upper respiratory tract but most of them have distinctive clinical and morphologic features or readily demonstrable causative agents. Of these, rhinoscleroma, rhinosporidiosis, coccidioidal granuloma, leprosy, leishmaniasis, granuloma venereum and glanders could almost certainly be excluded. Despite certain similarities to granulomata caused by yeasts and filamentous fungi, organisms of the types responsible for the more common mycotic infections such as blastomycosis and actinomycosis could not be found.

One granuloma which may affect the upper respiratory passages[1, 4, 5, 6, 9, 12] could not be dismissed so readily from consideration of the possible etiology. While sporotrichosis is commonly a disease of the skin and lymphatic structures it sometimes affects deeper tissues and organs. Cases have been described, with or without lesions of the skin, and with involvement of muscles, bones, joints, and various viscera and mucous membranes.[2, 4, 8, 10, 13, 14, 15] Such lesions are notoriously resistant to therapy with iodides, as were the lesions in the case presented. Illustrations and descriptions of mucosal sporotrichosis, especially the classic descriptions of de Beurmann and Gougerot,[4] are very like those in this case. These authors stressed the mixture of syphiloid, tuberculoid and ecthymatoid features in the inflammatory reactions and the difficulty of demonstrating spores. Others[3, 11] have stressed the same difficulty with all save superficial sporotrichotic abscesses.

Obviously, a positive diagnosis of sporotrichosis cannot be made in this

case. Morphologic evidence alone cannot be more than suggestive. The failure to obtain proof by culture on suitable medium or by inoculating animals must be cited. It should be noted, however, that it was extremely difficult to obtain suitable inoculum from the deep-seated lesions through the narrowed nasal passages. Too, it may be argued that the agglutination test may not have been specific. However, the titer of 1:320 was notably higher than those reported with control sera, or obtained in cross-agglutination tests with sera from patients with other mycotic diseases.

SUMMARY

A case is reported of a patient with a marked nasal deformity due to a granuloma of unknown etiology.

Most of the common and rare granulomata known to affect the mucous membranes of the upper respiratory passages could be excluded from consideration of the possible etiology.

The histopathology of three biopsies from the nasal mucosa of this patient, secured at widely separated intervals, was more like that of sporotrichosis than of other known granulomata.

While proof of the etiology is lacking, the clinical and morphologic features warrant characterizing this as a sporotrichosis-like granuloma.

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VARICOCELE AND ITS TREATMENT

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IN A TEXT-BOOK on the Practice of Surgery by Samuel Cooper,[1] in 1828, the term "varicocele" implied nothing more than an unnatural dilatation of the blood vessels of the scrotum, and was considered a disease of no importance. The term "circocele" was applied to the condition that is to-day commonly known as varicocele. It was described as a varicose distention and enlargement of the spermatic veins. Cooper also stated that it frequently occasioned great uneasiness and sometimes a wasting of the testicle, and was usually limited to that part of the spermatic cord below the abdominal ring. This fulfills the description in text-books of to-day, except that one may add there is a lengthening of the veins, that it occurs most frequently in young, unmarried adults, and is on the left side in 90 per cent of the cases.

Anatomy.—The spermatic veins on each side issue from the testis and epididymis and form the pampiniform plexus. This plexus is one of the constituents of the spermatic cord and consists of ten or twelve veins, most of which lie anterior to the vas deferens. For practical considerations, the plexus can be arranged in three groups: (1) The most anterior, which has in its midst the spermatic artery; (2) the middle, which has the vas deferens with its accompanying lymphatics and nerves; and (3) the posterior, composed of those veins which pass upward from the tail of the epididymis. The anterior group is the one first affected, or, if the dilatation affects all the veins, it is the group most extensively involved. The pampiniform plexus passes upward, unites within a short distance of the internal inguinal ring to form the spermatic veins, and ascends with each corresponding spermatic artery. Shortly before their termination, the veins unite to form one stem, which on the right side opens at an acute angle into the inferior vena cava below the renal vein, while on the left side it opens almost at a right angle into the lower border of the renal vein. According to Piersol,[3] the spermatic veins proper possess no valves, but there is usually a pair at the entrance of the right vein into the vena cava. In the stems of the pampiniform plexus, however, valves are usually found, but they are very frequently insufficient. An operation has been described by W. Turner Warwick[9] in which he excises only the involved stems and leaves a channel containing the competent valves.

Etiology and Classification.—Two types of varicocele are recognized: (a) Spontaneous, idiopathic, or primary; and (b) secondary or symptomatic. Seeondary varicocele results from spermatic vein obstruction by intra-abdominal tumors, most often of the kidney, but occasionally large carcinomata

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of the pelvirectal region. The sudden appearance of a right-sided varicocele is suggestive of an abdominal tumor and, according to Bates,[4] varicocele is a symptom in 30 per cent of kidney tumors. Varicocele of obstructive origin can be diagnosed by placing the patient in the prone position, at which time one can note that the veins do not readily empty themselves, as in the primary type. Removal of the obstructing tumor mass constitutes the treatment.

Primary varicocele is the type commonly seen. Usually the etiology is obscure or unknown. Age apparently is a factor, because it occurs in young individuals during the period of greatest sexual potentiality; nearly all are unmarried and have opportunities for sexual relief inadequate to their desires, which serves to perpetuate a constant genital congestion. Abuse by sexual excesses or masturbation may also result in this condition. Although most young adult males are subjected to sexual influences conducive to chronic pelvic congestion, only about one in ten develops varicocele. For years, the left-sided preponderance has been explained on an anatomic basis; namely, that (1) the left vein opens at an acute angle into the vena cava; (2) the left vein is destitute of valves at its opening into the renal, while the right one usually possesses a pair at its orifice; (3) the left vein in its course up the abdominal wall lies beneath the sigmoid colon, while the right has only coils of small intestine with their more fluid contents; (4) the left testicle hangs lower and the left spermatic vein is longer. Vascular dysfunction is more common in old men in whom varicocele is rarely encountered but in whom varicosities and hemorrhoids are frequent. The fact that the left spermatic vein passes under the sigmoid, which may obstruct the vessel, has been advanced as a cause of varicocele, but chronic constipation with an overloaded sigmoid is characteristically a disease of advancing years. The actual cause is unknown, but chronic passive genital congestion is probably the underlying factor, as is demonstrated by the disappearance of most varicoceles and the symptomatic cure of many with the assumption of normal sex relationship of marriage.

Symptoms.—Occasionally varicocele may follow violent strain and be accompanied by severe local pains. Usually the onset is gradual. Many patients have varicoceles of considerable size without symptoms; occasionally they complain of the inconvenience of the relaxed scrotum and low hanging testicle, especially in warm climates. Often the symptoms are those of sexual neurasthenia, along with a variety of generalized aches and pains out of all proportion to the objective findings. Of the uncomfortable stimuli produced by varicocele, the most frequent is a dragging sensation in the testicle referred to the groin, lower abdominal quadrant, or lumbar region; a dull aching pain in the testicle may be constant, aggravated on exercise.

Diagnosis.—On examination, one notes a relaxed scrotum and a low hanging left testicle with the tortuous veins often visible. On palpation there is the typical feeling likened to a bag of earthworms. These findings can rarely be confused with any other condition. A large hydrocele or

hernia may obscure the varicocele. The testicle may show some atrophy. Perhaps the only condition it may be confused with is omental hernia. A sure method of distinguishing the two complaints is as follows: Place the patient in a horizontal position and empty the swelling by pressure on the scrotum; then place the finger firmly upon the upper part of the abdominal ring and have the patient rise; if it is a hernia, the mass cannot reappear as long as the pressure is continued at the ring, but if it is a varicocele, the swelling returns with increased size because the return of blood into the abdomen is prevented by the pressure.

Treatment.—Samuel Cooper,[1] in his treatise on the Practice of Surgery, states that a radical cure can seldom be effected. He advocates supporting the testicle with a suspensory bandage and if necessary the use of cold and alum lotions; also, that the blood be repeatedly taken away by means of leeches. From his observations, and the reports from very good authors, pointing out the severe complications which may and do result from varicocelectomy, we are apparently considering the operation too lightly, as too many such operations are being performed. According to Campbell,[10] Douglas, in a careful follow-up in 106 of 305 cases operated upon for enlistment in the Army, found 48 per cent normal after a postoperative intermission of many months, 39 per cent had hydrocele, and four had atrophy. This is not a very cheerful report when one considers surgical treatment.

Therapeutically, three types of varicocele are recognized: The first is asymptomatic anatomic varicocele, which may be either large or small. In this type of case, operation is not indicated; however, we do operate upon some of these cases when sent into the hospital by ship's physicians who refuse to pass the individuals for duty on boats. In the second type of case the patient presents himself with a scrotal enlargement and a feeling of weight or a dragging sensation, either in the testicle or referred to the cord, groin or loin. This is the type of case in which operation is definitely indicated; however, the number of such cases presenting themselves each year, with symptoms severe enough to warrant operation, is small, perhaps not over five or six. In the third type, unfortunately, fall a large number of the cases. These are the individuals who have a small varicocele with a variety of symptoms and anxiety regarding the integrity of their sexual apparatus. This type of case requires the utmost consideration and is entitled to some patience on our part and an explanation of the mechanism of varicocele, with assurance that the condition is not a serious one. Even then, we are forced to operate upon some of them because they will not or cannot help themselves.

Injection treatment is advocated by some, who state that it is practically 100 per cent successful and that it avoids the two ever present possibilities which may follow operation, namely, atrophy of the testicle and secondary hydrocele. Different methods are described, but each points out that perivascular infiltration will not effect a cure and secondary injections are difficult. Although injection may achieve the same effect as the ordinary surgical

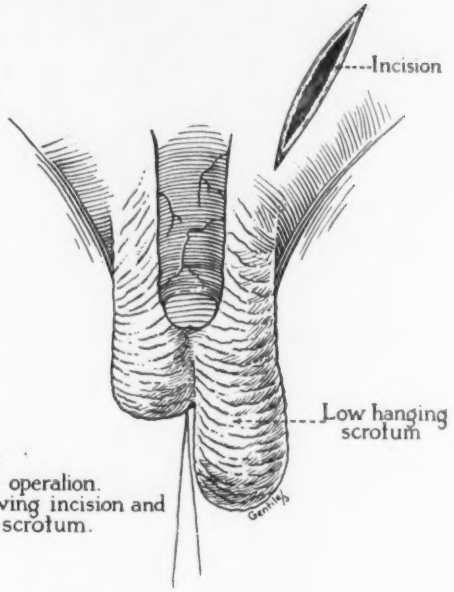

FIG. 1.

Before operation.
Showing incision and low scrotum.

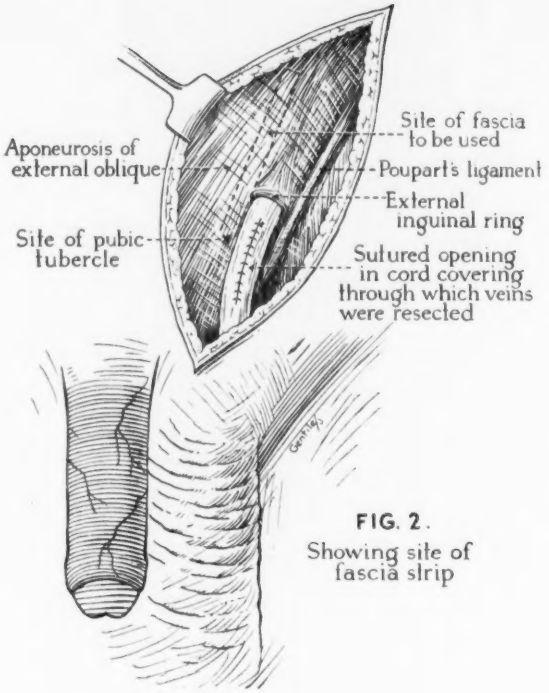
Site of fascia to be used
Aponeurosis of external oblique
Poupart's ligament
External inguinal ring
Site of pubic tubercle
Sutured opening in cord covering through which veins were resected

FIG. 2.

Showing site of fascia strip

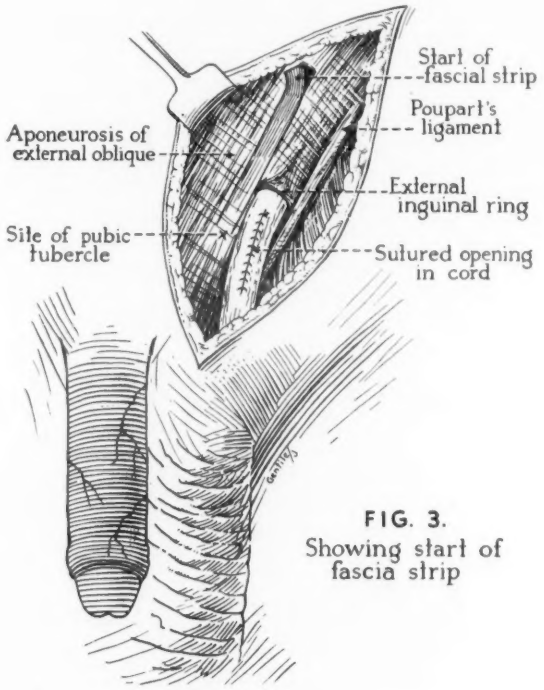

FIG. 3.
Showing start of fascia strip

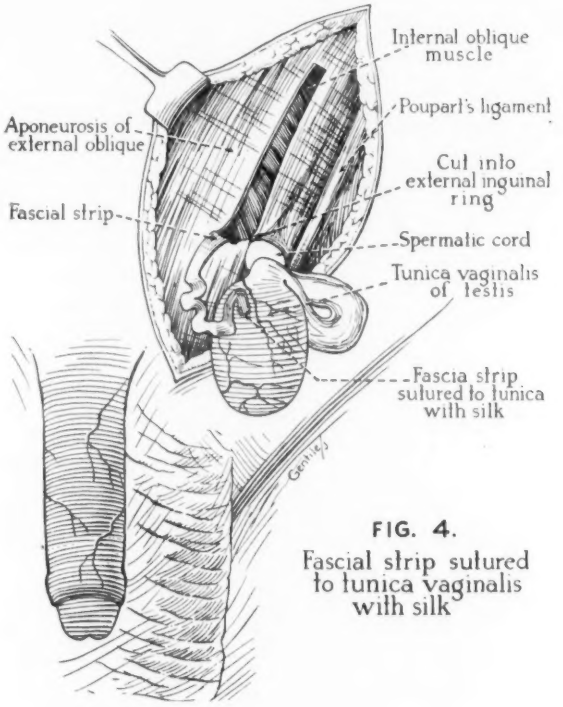

FIG. 4.
Fascial strip sutured to tunica vaginalis with silk

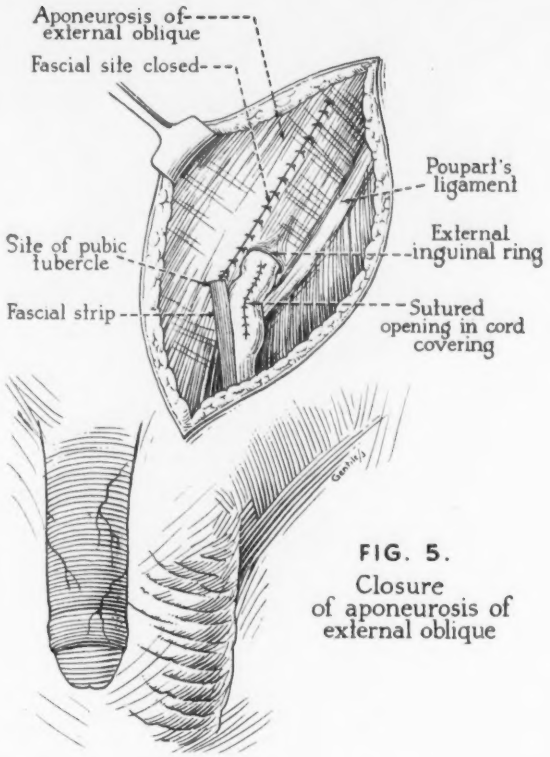

FIG. 5.
Closure of aponeurosis of external oblique

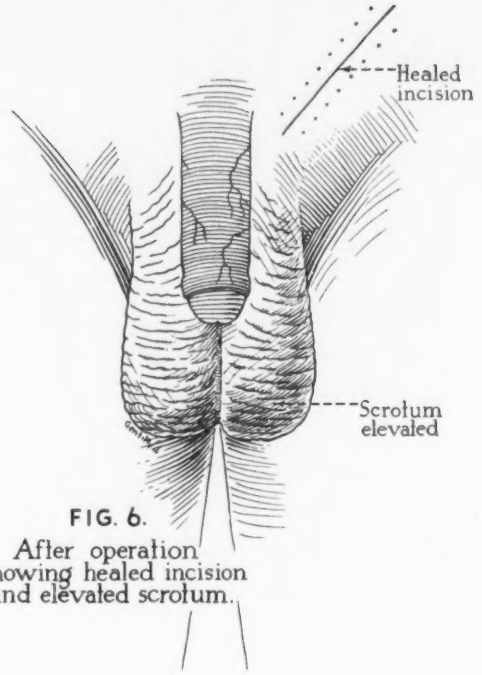

FIG. 6.
After operation
Showing healed incision and elevated scrotum.

PLATE I.—Showing the various steps of the operative procedure employed in the suggested modification of Londres' operation for varicocele (Hospital News, 4, No. 16, 1937).

operation, the amount of the plexus obliterated is not so easily controlled by injection as by operation. I think that we have all seen patients who are better satisfied with the final results following operation than we are ourselves. In this regard, according to Warwick,[9] Carver and Nitch reviewed 100 cases and found that 20 still suffered pain and four were even worse after the operation; also, in spite of the fact that a hydrocele was present in 23, fibrosis of the testicle in 55, and atrophy in 21, it was found that at least 70 of the patients were comfortable and well satisfied with the operation. Unquestionably, if this represents a satisfactory standard of amelioration in this condition, it may eventually prove that injection treatment may very well serve the purpose. In the absence of this knowledge it is my opinion that, in carefully selected cases, operation is the method of choice.

Operative Procedure.—Numerous procedures have been resorted to in the treatment of varicocele, but the usual operations performed can be placed in two groups: (1) Those designed to act directly on the varicose veins of the pampiniform plexus; and (2) those which seek to promote a simple suspension of the varicose plexus, either by resection of the scrotal sac or by simple suspension of the testis. Until three years ago, the method I employed was anchoring the distal end of the cut anterior pampiniform plexus to the external ring (Vincent's operation), together with resection of the scrotum when atony was marked. The results were satisfactory, but this did not always give permanent suspension of the testis. In January, 1934, Londres[8] reported an operative technic for suspension of the testicle which is easy, quick, and apparently harmless and, it appears to me, more than any other procedure offers possibilities for an efficient permanent suspension. The following is a description of the operation: It consists in suspension of the testicle by means of a flap cut from the fascia of the external oblique muscle, which is folded downward (Figs. 2 and 3), its pubic insertion remaining attached and its loose end being fixed to the testicle just below the ischiopubic bone. The opening made in the fascia of the external oblique is sutured after one has assured himself that the external inguinal opening has retained a proper diameter.

The resistance of the strip of fascia, together with the fact that it will not stretch, guarantees the lasting suspension, counteracting the distention due to dependency and relieving the weight on the vas, the common cause of cord pain. We have been using a strip of fascia about one-quarter of an inch wide and two inches long, anchoring the free end to the upper portion of the tunica vaginalis with silk (Fig. 4). In addition to the suspension, we have been removing a section of the anterior pampiniform plexus, if markedly varicosed, due care being given not to injure the spermatic artery and not to interfere with the middle or posterior portion of the cord. In doing this we would rather err by not removing enough veins than too many, as we believe that the return flow of blood from the testicle is important to prevent complications.

The objection that presents itself to this operation is the possible trauma to the testis and tunica which is supposed to be one of the causes of hydrocele formation. During the past six years we have operated upon 44 cases in this manner with very good results and without any ill effects. Over half of these cases have been observed for a period of a year or longer, and it was found that they were completely relieved of symptoms, did not have any hydrocele and the fascia support was holding the testicle in the proper position. It is questionable whether it excites an inflammatory process already present, as Campbell[10] states that the specific gravity of the fluid is that of an inflammatory exudate rather than a transudate resulting from vascular disturbance.

CONCLUSIONS

The etiology of primary varicocele is usually obscure. It occurs in young individuals, rarely in men of advanced years, when vascular dysfunction is more common. Marriage commonly effects a cure. The diagnosis is usually easy and rarely mistaken for any other condition. Varicoceles have been grouped into three types, according to the classification of Campbell,[10] which appeals to me as being a very good method in selecting cases for operation. The common complications of operative treatment are hydrocele and atrophy of the testicle, and in some reports these complications seem to be rather high. Cases for operation should be carefully selected and the operation should not be considered a minor procedure, care being taken in technic and identification of various structures which possibly may be a factor in producing the above complications. If the case is not one for operation, the patient should not just be given a suspensory, which is often unsanitary and ineffectual, but his condition should be explained to him as not being a serious one and one that will not affect him in any way. The operation of choice is one of the suspension type. The patient usually remains in bed for five to seven days, and wears a testicular support for 30 days.

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INDELIBLE PENCIL INJURIES TO THE HANDS

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INJURIES to the hands and fingers by the points of indelible pencils are fairly infrequent, but the characteristic chain of events which follows them warrants the occasional report of a case and justifies reemphasis of their importance. The severely irritative and destructive properties of aniline dyes, when introduced into the eye by the "lead" of indelible pencils, was recognized many years ago by the ophthalmologists (Gräflin,[21] Kuwahra,[25] Vogt,[38] Dejean,[12] Marshall,[27] and Bride[8]). The eczematous and acneform eruptions, papillary growths and, very rarely, epithelioma of the skin from aniline dyes, are well recognized by the dermatologist (Sachs[35]). Bladder carcinoma in aniline dye workers is a classic example of malignancy due to chemical irritation (Rehn[34a]). Puoz,[34] in a general review of the subject, noted one patient who suffered severe injury from the introduction of an indelible pencil into the urethra, and Ilkoff[22] reported on the effects of indelible lead on the gastrointestinal tract of a patient who was given, as a joke, a beefsteak containing a piece of indelible pencil.

Sigmund Erdheim,[14] in 1914, was the first to report indelible pencil wounds of the hand. Glass,[20] in 1922, first called attention to the general toxic manifestations of indelible injuries. Excellent reviews of indelible pencil injuries have been published by Anglesio,[1] Arce,[2] Bettazzi,[4] Bianco,[5] Bravo and Canedo,[6] Bull,[9] Buzzi, Costa and Derqui,[10] Dalquen,[11] Erdheim,[14] Gierlich,[17] Glass and Krüger,[19] Iselin,[23] Marsiglia,[28] Milch,[31] Perez,[33] Puoz,[34] and to these papers the reader is referred for more extensive discussion.

The "lead" of indelible pencils is made up of inert substance or filler, usually graphite, an inert binding substance, and a dye which gives the color and "indelible" property to the "lead." The dye has been proven to be the toxic agent (Kuwahra,[25] Vogt,[38] Erdheim,[14] Glass and Krüger,[19] and others); the other components behave simply as inert foreign bodies and differ in action in no way from ordinary graphite pencil which may lie buried in the tissues for years (60 years in the case of Glass,[20] 1931).

The dyes used belong to the triphenylmethane, diphenylmethane and diphenylamine groups, the most frequently used being methyl violet of the triphenylmethane group. The toxicity of the dyes is associated with their reaction; they become increasingly toxic with increasing alkalinity, and may be listed in order of increasing toxity as follows: Green, yellow, red, brown, blue, violet, and black. It has been pointed out by Vogt,[38] that the difference

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in toxicity is one of degree only, and that all cause chemical necrosis. It would seem that they produce a disturbance in cellular metabolism due to the chemical affinity of the alkaline dye for nucleic acids in the nuclei of the cells.

When indelible "lead" is introduced into the tissues, the dye at once begins to dissolve, and leads to a necrosis of the adjacent cells. As the highly concentrated dye is carried farther outwards the area of necrosis enlarges and all tissues in its path are involved—the skin and its appendages, connective tissue, fat, muscle, nerves, cartilage and bone. Where blood vessels are subjected to high concentration of the dye, they become totally necrotic and thrombosed; farther away, where the dye is less concentrated, the necrosis may involve only the adventitia, while the media and intima may show round cell infiltration and proliferation. It is possible, as Ettore[15] has suggested, that this thrombosis and associated secondary infection may be factors in producing the extensive necrosis which may involve whole digits or phalanges.

A protective wall of leukocytes is thrown up about the advancing process, but it is pushed back farther and farther until the dye is diluted beyond the point of toxicity, has been altered by local metabolism, or has been carried away by the blood and lymph. Then the process comes to a standstill, the protective wall liquefies, and the necrotic central mass is cast off, leaving an ulcer which heals slowly by granulation. Superficial areas may separate and heal spontaneously in five or six weeks. If the dye has penetrated deeply, months or even years may elapse. Occasionally, a very slight injury may result in tattooing. Sharlit[36] has recorded one instance in which a melanoma developed in such a tattooed area.

The local clinical manifestations of indelible wounds of the hand may be minimal. At the time of the injury there is some pain which persists for an hour or so, and along with this there is edema of the surrounding tissues. If the injury is near a nerve there may be sensory loss over its peripheral distribution. As the dye becomes more widely diffused the reaction becomes more marked, the pain may recur, and may radiate distally or peripherally; but it is remarkable that pain is rarely the presenting symptom. The puncture wound continues for a long period of time to secrete a purple fluid which discolors the dressings.

If the fistulous tract is simply incised and an attempt made to remove the lead, the incision refuses to heal and the process becomes an ulcer with violet base and borders. Occasionally, if the penetration has been quite deep, the puncture wound heals and a tumor-like mass develops which, if incised, leaves a purple ulcer that persists for weeks or months before healing occurs.

General symptoms are not always present, but in about 20 per cent of cases (Puoz) complaint is made of headache, malaise, anorexia, gastro-intestinal upset, and general weakness. Such symptoms do not often come on for several weeks after the injury, may be associated with fever and increased white cell count, and, as in a case reported by Gartenmeister,[16] icterus may develop. Torraca[37] found experimentally that although the kidneys showed the most damage, the liver was also affected by methyl violet; and Glass[19]

found that the lungs, heart, liver, spleen, and kidneys of mice receiving methyl violet, were markedly congested and that the liver showed capillary hemorrhages and leukocytic infiltration. Gierlich,[17] on postmortem examination of a premature infant who had been given indelible lead, found toxic changes in the parenchymastous organs. He showed experimentally that the dye is absorbed as a colorless substance into the blood stream and acts as a protoplasmic poison, producing anemia, cloudy swelling and accumulation of fat globules in the cells. In one experiment an acute yellow atrophy of the liver was produced.

In one of our cases (Case 2) anorexia, weakness, lassitude and a brief postoperative febrile reaction seemed due to toxemia from the dye rather than to a concurrent local infection. This was particularly striking since the toxic symptoms did not develop until seven weeks after the injury, and the anorexia and lassitude persisted for several weeks after the local process had subsided.

The treatment of indelible pencil injuries is complete, immediate excision, care being taken that no tissue stained by dye is left behind. If this can be effected at once, the wound may be safely sutured with assurance of primary healing. The "lead" should never be picked out with forceps, which breaks up the foreign body and scatters bits of the dye throughout the tissues. In the late case, removal of dye-stained tissue is also indicated; but where bones, tendons and other essential structures are involved, complete excision may be impossible. In such instances the wound is left open and allowed to heal by granulation. In other instances complete excision and primary closure may be accomplished even as late as two and one-half months after injury (Case 1). At times (Jerusalem[24]), the necrotizing action may be so severe and extensive that amputation is necessary.

The systemic reaction is due to absorption of the dye or of some of its products. It has been shown that the dye is very slowly excreted by the kidneys. However, the common occurrence of gastro-intestinal symptoms and an occasional instance of icterus would seem to indicate that the liver must also play a rôle in the excretion of the dye. For this reason, it seems logical to administer glucose and prescribe a liberal carbohydrate diet when toxic symptoms occur.

CASE REPORTS

Case 1.—Cook County Hospital, Nos. 1689466, 1690535 and 8873: J. S., male, age nine, injured the dorsum of the right index finger with an indelible pencil, December 3, 1937. He squeezed the wound and made it bleed, but did not remember whether he succeeded in removing the point of the pencil. The following day the finger became swollen and there was discharge of bluish fluid, but there was no pain or tenderness. Four days after the injury the patient was admitted to Cook County Hospital where the wound was simply cleansed and dressed and the patient was instructed to report to the Hand Clinic for dressings, where he reported three days later, December 10, 1937, at which time there was noted a fusiform swelling of the finger and an ulcer about 3 Mm. in diameter (Fig. 1), from which thin, bluish fluid exuded. The finger was cleansed and splinted and the patient advised to apply dry heat at home.

He was readmitted to the hospital, three days later, with a moderately severe infection which subsided quite rapidly under cleanly care and moist heat. Following discharge from the hospital he reported for dressings until February 19, 1938, at which time the sinus had healed, leaving a blackish, discolored area about 1 cm. in diameter. He was again admitted to the hospital and the finger opened, under a general anesthetic. The skin and subcutaneous tissue, over an area of approximately 1 cm. in diameter, were purple and gelatinous, and the extensor tendon over the distal interphalangeal joint was soft and necrotic. All involved tissue was excised, the wound sutured, and the finger splinted in hyperextension. The wound healed by primary intention in about ten days. The splint was left on for five weeks in order to allow firm healing of the extensor tendon defect, and a good functional result was obtained (Fig. 2 A and B).

The microscopic examination of the excised tissues showed, in the skin, a small accumulation of round cells with single foreign body giant cells embedded deep in the reticular layer of the dermis. On section through the tendon there is a dense, firm collagen

FIG. 1.—Case 1: Indelible pencil injury to dorsum of index finger. Before excision.

A B

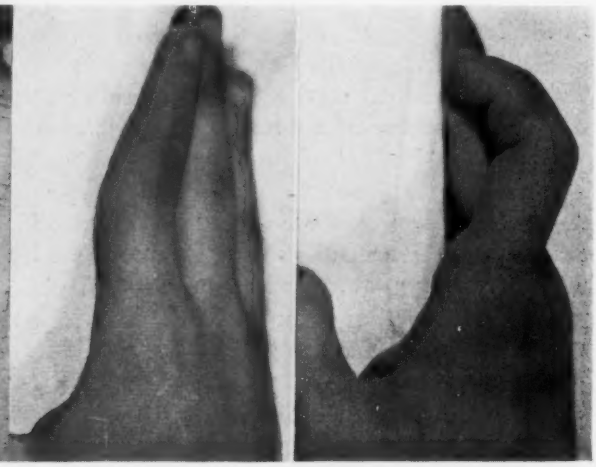


FIG. 2.—Case 1: A and B. Indelible pencil injury to dorsum of index finger. Return of function after excision and suture.

connective tissue in which are found spicules of coal-black pigment. In one area this pigment is surrounded by round cells and single foreign body giant cells" (Alex. B. Ragins, M.D., Pathologist).

Case 2.—Passavant Memorial Hospital, Nos. 41849 and 43322: R. T., male, age 17, was admitted to the hospital, April 27, 1939, with the history of, seven weeks previously, having had the lead of an indelible pencil accidentally driven into the palm of the right hand. He had been taken at once to a physician who extracted the piece of lead and applied moist packs. During the first week after the injury there was considerable swelling about the wound, there was an elevated temperature, local redness, and pain on motion. There was some purplish discharge from the wound. During the second week the symptoms subsided, and by the end of this week the puncture wound had healed. During the ensuing five weeks the swelling receded, pain and tenderness disappeared, and the patient regained complete use of the finger. There remained, however, a small grayish spot where the pencil point had entered. Two days previous to admission to the hospital, and seven weeks after the original injury, the swelling, pain and tenderness recurred, and hot, moist compresses were again applied. The process, however, became steadily worse and he was admitted to the hospital with a temperature of 100.4° F., and

a white cell count of 12,630. Examination showed a tense, uniformly swollen right index finger, held in semiflexion. In the palm over the region of the second metacarpophalangeal joint was a small sinus with grayish borders exuding grayish liquid (Fig. 3 A and B). Pressure over the course of the tendon sheath produced pain, as did both flexion and extension of the finger. There were no enlarged lymph nodes in the epitrochlear or axillary regions and no evidence of a lymphangitis. *Clinical Diagnosis:* Suppurative tenosynovitis secondary to indelible pencil injury. Drainage was immediately established.

Operation.—Under general anesthesia, a transverse incision was made over the proximal culdesac of the tendon sheath, directly through the sinus tract. A second, longitudinal, incision was made along the radial border of the finger. A grayish, purulent exudate was found both in the culdesac of the sheath and in the sinus tract.

A B

FIG. 3.—Case 2: A and B. Indelible pencil injury to right palm, with perforation of the tendon sheath, seven weeks previously. Suppurative tenosynovitis from secondary infection through sinus tract.

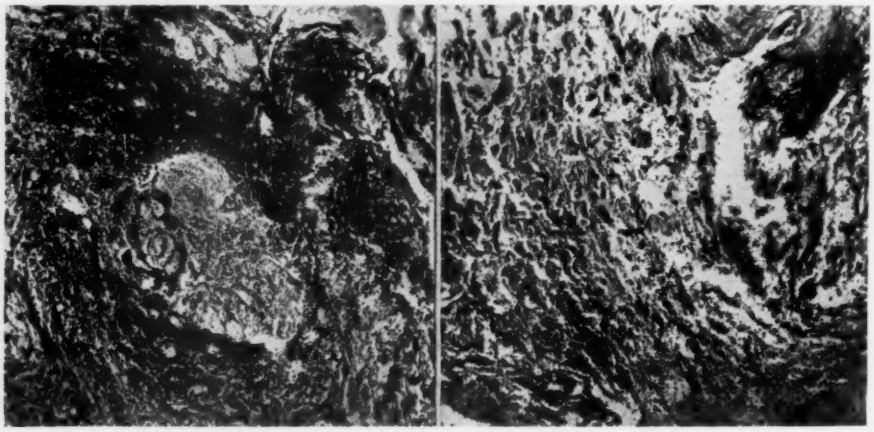
Bacteriologic examination of this exudate revealed a pure culture of hemolytic staphylococcus aureus which grew well both aerobically and anaerobically. Upon cutting through the skin at the site of the sinus, there was encountered a gray, granulomatous mass of tissue, about 2 cm. in diameter, which extended to the fibrous tendon sheath which was also streaked with gray. Upon opening the sheath, seropurulent fluid was evacuated, and the tendons within the sheath showed grayish and black streaks. The fibrous tendon sheath in the finger also showed these grayish streaks and the vincula were similarly stained. There was slight violet coloration of the liquid in the digital part of the sheath. The granulomatous tissue and some of the gray tissue were removed, but complete removal was not attempted because of the complicating infection.

The postoperative course for the first few days was somewhat stormy and presented a picture which suggested a toxemia not entirely compatible with the evident infection.

Although the boy complained of pain in the finger, hand and forearm, there was no evidence of a spreading infection, the swelling was confined to the finger and metacarpophalangeal joint, and there was no lymphangitis, although the axillary nodes were tender. At no time did the temperature rise over 100.4° F. He developed upper abdominal distress and diffuse tenderness over the whole upper abdomen, anorexia was marked, he was listless and apathetic. He was not jaundiced, though the icterus index was 7.5. This situation persisted for about eight days, during which time he received large amounts of fluid, and 2,000 cc. of 10 per cent glucose was administered intravenously on two occasions.

After the eighth postoperative day the temperature came down to normal and the general condition improved except for the listlessness and anorexia which persisted for some six weeks. The incision healed slowly following the discharge of two large plugs of gray necrotic tissue, and was complete on May 27, 1939, one month after operation.

Pathologic Examination.—Microscopic: Dr. Frank B. Queen. The excised tissue



A B

FIG. 4.—Case 2: Photomicrograph of tissue removed at first operation. (A) Tissue from central portion of necrotic area shows dense mass of pigment and absence of any viable cells. (B) Tissue from more peripheral portion, still filled with pigment, some viable nuclei present. (×105)

showed a "necrobiosis of subcutaneous tissue due to foreign body (Fig. 4 A and B). The tissue is composed of necrobiotic material in which the hazy outlines of cells are seen, and apparently there has been a good deal of inflammation prior to the development of the necrosis, since in many fields the tissue seems excessively cellular. The material now stains purplish-blue and vague outlines of nuclei are seen in much of it. In addition, there are many masses of black pigment of variable size, which, when examined for distribution, seem to be more prevalent in the zones containing hyaline connective tissue than anywhere else. Sections from one of the blocks are better preserved than the others and, here, mononuclears seem to be the predominant type of cell."

Subsequent Course.—On July 26, 1939, two months after the incision had healed, and the boy had begun to work driving a car, a tender swelling appeared at the lateral end of the transverse palmar incision. It proved to be a small subcutaneous abscess which was opened and drained. Since it lay under the scar of the previous incision, occasion was taken to remove a thin piece of grayish skin and subcutaneous tissue for microscopic examination. The abscess healed rapidly following drainage and, except for its coincidental location with the previous injury, presented nothing extraordinary.

The microscopic sections are of interest since they show the hyperplastic changes in

the skin which may follow indelible injuries. Doctor Queen reported that "the epithelium is somewhat hyperplastic and hyperkeratinized (Fig. 5). Beneath it is the rather heavily vascular corium. There are masses of dark-staining, granular, blue-black pigment. None of these appears to be phagocytized as far as can be definitely determined. They lie in the interstices of the tissues and occasionally there seems to be some disintegrating cytoplasm about some of them. The connective tissue of the corium elsewhere is rather edematous and quite well vascularized. There is perivascular cuffing with lymphocytes and mononuclears."*

FIG. 5.—Case 2: Photomicrograph of epithelium removed at second operation, showing moderate hyperplasia and hyperkeratinization. Pigment diffusely scattered throughout corium, no evidence of phagocytosis. (X60)

* The indelible pencil in this case came from one of the well-known foreign pencil manufacturers. Chemical tests carried out on the pencil lead, by Dr. Chester Farmer, Professor of Chemistry, Northwestern University Medical School, indicated that the dye which it contained was methyl violet. An inquiry, sent to the New York office of the firm which manufactured the pencil, was answered briefly and noncommittally, with the assurance that to the best of their knowledge no injurious substance was contained in the pencil, but no information was given as to the actual dye used. It is interesting to note that Kuwahra, Erdheim, and others who experimented with similar pencils, had no hesitancy in naming the manufacturers and that the name of this firm appeared in the literature (Kuwahra) in this connection well over 35 years ago.

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AMEBIASIS CUTIS

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THE PATHOLOGIC PROCESSES resulting from infestation with Endameba histolytica have attained considerable surgical significance. Althought amebiasis is usually considered to be a tropical disease, manifestations of it have been reported from all sections of the United States. Craig[1] examined 49,336 people from all parts of the United States for amebae and found 5,720 (11.6 per cent) to be infested. Ochsner and DeBakey[2] estimate that 500,000 to 1,000,000 people in this country are so affected.

The most common manifestations of amebiasis are the intestinal lesions and hepatic abscess.

One of the less common but most serious lesions due to amebae is ulceration and gangrene of the skin and subcutaneous tissues. Two such cases have been encountered in the Vanderbilt University Hospital. Only one of these cases recovered, which was due to the prompt recognition of the cause of the gangrene and the institution of specific treatment soon after entrance to the hospital.

Twenty-eight cases of gangrene and ulceration of the skin due to Endameba histolytica have been collected from the literature. All of these cases had associated visceral lesions and presented definite evidence that the lesions were due to Endameba histolytica. Reviewed cases not fulfilling these requirements are not included.

Ngai and Frazier[3] reviewed the literature in 1933. These authors included 27 cases in their report. Several of their cases which do not fulfill the above requirements are not included in this review. Since 1933, only six additional cases have been reported.

Nasse,[4] in 1891, was the first to describe this condition, but the term "amebiasis cutis" was first applied by Engman and Heithaus[5] in 1919. Nasse's case followed drainage of a liver abscess but motile amebae were not identified. Engman and Meleney,[6] in 1931, reported two cases of amebiasis cutis in which the characteristics of the Endameba histolytica were definitely identified. Meleney and Meleney[7] reported a case of extensive ulceration of perianal region in which complete bacteriologic as well as protozoologic studies were carried out. In this case the presence of the micro-aerophilic nonhemolytic streptococcus was definitely ruled out, showing that the skin changes were due entirely to Endameba histolytica.

As has been pointed out by Engman and Meleney,[6] the published cases fall into four groups. The classification is as follows:

(1) Cases following drainage of amebic abscess of the liver.

TABLE I

SYNOPSIS OF 28 CASES OF AMEBIASIS CUTIS COLLECTED FROM THE LITERATURE

No.	Author	Age	Sex	Previous Dysentery	Site	History	Smear	Microscopic Examination	Stools	Treatment	Course
1	Nasse, D.,[4] 1892	60	M.	No	Abd. wall	Abdominal pain; palpable epigastric mass. Surgical drainage liver abscess, followed in 7 days by progressive gangrene abdominal wall to area 4x5 cm.	Neg.	Pos.	Not exam.	Palliative. No specific therapy.	Progressive weight loss; high fever. Died.
2	Menetrier, M. P., and Touraine, M. H.,[15] 1908	23	M.	No	Abd. wall	Surgical drainage liver abscess, followed by progressive necrosis skin around incision.	Pos.	Neg.	?	?	Died.
3	Bassires, F.,[12] 1911	52	M.	No	Chest wall	Surgical drainage liver abscess, followed by gangrene chest wall. Lesion at time of death, 13x15 cm.	Pos.	Neg.	Pos.	Local application of antiseptics.	Progressive necrosis; marked drainage; profuse hemorrhage drainage site. Died.
4	Carini, A.,[22] 1912	37	M.	Yes	Abd. wall	Surgical drainage liver abscess. Smears positive for amebae. Drainage followed by progressive gangrene abdominal wall to area 10x15 cm.	Pos.	Neg.	Neg.	Surgical incision necrotic tissue to rectus muscle. Local application of quinine sulph.	Excised area healed. Well.
5	Carini, A.,[22] 1912	30	M.	Yes	Abd. wall	Surgical drainage liver abscess followed 20th p.o. day by gangrene edges of wound, and 27th p.o. day by extensive necrosis to rectus muscle, area 10x8 cm.	Pos.	Pos.	?	?	Progressive necrosis. Died.
6	Daborn and Heymann,[25] 1912	38	M.	Yes	Abd. wall	Surgical drainage liver abscess followed 10th p.o. day by necrosis of edges of incision.	Pos.	Pos.	Pos.	Actual cautery. Local application silver nitrate.	Progressive necrosis abdominal wall to lesion 3.5x6 cm.; high fever; marked diarrhea. Died.
7	Heymann and Ricou,[28] 1916	?	?	?	Abd. wall	Surgical drainage liver abscess. Necrosis skin edges; progressive gangrene abdominal wall following 11th p.o. day.	Pos.	?	?	Intravenous emetine hydrochloride. Actual cautery. Irrigation with quinine sol.	Local process ceased to spread. High fever continued. Died.
8	Kofoid, Boyers and Swezy,[32] 1924	?	?	?	Abd. wall and l. ex.	Surgical drainage liver abscess. Edges incision erythematous; concomitant erythematous spots lower extremities.	?	Pos.	?	?	Died. Autopsy: Sections from skin lesions showed Endameba histolytica.
9	Heimburger, L. F.,[27] 1925	39	M.	No	Rt. flank	Spontaneous rupture mass right flank. Persistent discharging fistula. Development ulcer site of drainage. Sinus tract communicated with cavity in liver.	Pos.	Pos.	Neg.	Emetine hydrochloride.	Amebae disappeared from lesion. Ulcer healed by granulation. Well.

TABLE I (*Continued*)

No.	Author	Age	Sex	Previous Dysentery	Site	History	Smear	Microscopic Examination	Stools	Treatment	Course
10	van Hoof, L.,[11] 1926	?	F.	Yes	Perianal reg.	Dysentery 10 yrs. prior to appearance of multiple ulcerations, with fistula, about anus.	Pos.	?	Neg.	Emetine hydrochloride.	Amebae disappeared from lesion, which rapidly healed. Well.
11	Tixier, Favre, Morenas and Petourand,[18] 1927	53	M.	Yes	Perianal reg.	Dysentery for years. For 6 yrs., ulcerated perianal skin lesions 6x7 cm. No demonstrable fistula.	Pos.	Pos.	Neg.	Emetine hydrochloride. Cautery excision.	Lesions healed rapidly. Well.
12	York and Adams,[33] 1928	?	M.	Yes	Abd. wall	Surgical drainage liver abscess. Necrotic skin and progressive gangrene abdominal wall.	Pos	Pos.	Neg.	Emetine hydrochloride.	Necrotic area separated. Edema and redness disappeared. Uneventful recovery. Well.
13	Cole and Heidman,[21] 1929	34	M.	No	Abd. wall	History and physical findings of acute appendicitis. Appendicectomy, followed on 9th p.o. day by necrosis about wound and spreading gangrene.	Pos. ?	Pos. ?	Neg.	Emetine hydrochloride.	Emetine had no effect upon lesions. Cure effected by cautery excision. Well.
14	Marwits and van Steenis,[29] 1929	?	M.	No	Abd. wall	Drainage appendiceal abscess followed by spreading ulcerative process abdominal wall. Lesion 24x12 cm.	Pos.	?	Neg.	Emetine hydrochloride.	Ulcer healed. Well.
15	Marwits and van Steenis,[29] 1931	?	M.	No	Abd. wall	Perforated cecum due to intestinal (?) amebiasis. Pericecal abscess with spread to abdominal wall.	Pos.	?	Neg.	Emetine hydrochloride.	Lesion healed. Well.
16	Engman and Meleney,[8] 1931	51	M.	—	Abd. wall	History intestinal obstruction. Celiotomy. Resection of hepatic flexure colon because of ulceration and obstruction. Fecal fistula 7th p.o. day. Necrosis abdominal wall 2 mos. p.o. Rapid spread of lesion to 12x15 cm.	Pos.	Pos.	?	Emetine hydrochloride.	Lesion healed. Died 9 mos. p.o. from peritonitis due to soiling from fecal fistula. Died.
17	Engman and Meleney,[8] 1931	34	F.	Muc. colitis 3 yrs. Yes	Abd. wall	Pain r. l. q. Celiotomy with rupture of mass in r. l. q. Necrosis wound edges progressing to area 10x10 cm.	Neg.	Pos.	?	No specific therapy.	Progression of gangrenous process. Died.
18	Cheng, C. C.,[25] 1931	25	M.	No	Abd. wall	Ruptured liver abscess 5 mos. prior to admission, followed by ulcer abdominal wall which progressed to area 14x16 cm. Had kala-azar.	Pos.	Neg.	Neg.	Emetine hydrochloride.	Lesion healed rapidly. Skin graft. Well.

19	Taylor and Hunter,[21] 1932	40	M.	No	Abd. wall	Drainage of abscess abdominal wall followed by progressive gangrene.	Pos.	Neg.	?	Emetine hydrochloride. Cautery excision.	Lesion subsided. Healthy granulations. Smears negative for amebae.
20	Kouri, Bolanos and Fuentes,[8] 1933	44	M.	Yes	Perianal reg.	Perianal fistula 10 yrs. Marked ulceration following incision and drainage.	?	Pos.	?	Deep x-ray therapy.	Well. Died. Autopsy: Sections showed amebae in skin of lesions of buttocks.
21	Ngai and Frazier,[3] 1933	30	M.	Yes	Perianal reg.	Ulcers perianal region 20 days prior to admission. Ulcers about anus 4 cm. Proctoscopic examination showed ulcers of rectal mucosa.	Pos.	Pos.	Neg.	Saline compresses 2 wks. without tendency to heal. Emetine hydrochloride. Yatren compresses.	Healing of lesion 10 days after institution emetine. Well.
22	Ngai and Frazier,[3] 1933	43	F.	No	Perianal reg.	Ulcerative lesions vulva and anus; condylomatous lesions urethral orifice. Scrapings of latter positive for spirochetes. Positive Wassermann. No response to antileutic treatment.	Neg.	Pos.	Neg.	Biopsy revealed amebae. Patient failed to return for treatment. No emetine given.	Not followed.
23	Ngai and Frazier,[3] 1933	46	F.	Yes	Perianal reg.	Fungating cauliflower mass, 8x6 cm., anal region. Mass excised.	Neg.	Pos.	Neg.		Not followed.
24	Crawford, S.,[14] 1933	40	F.	No	Buttocks	Extensive ulceration cutaneous surfaces of buttocks, present 4 yrs.	Pos.	Pos.	Pos.	Excision. Emetine hydrochloride.	Active lesions persisted.
25	Meleney and Meleney,[7] 1935	51	M.	Yes	Perianal reg.	Tender mass just lateral to anus, 1 mo.; rupture and discharge large quantity foul-smelling pus. Large ulcer over sacrum and buttocks.	Neg.	Pos.		Lesion excised. Emetine hydrochloride.	Well. Lesion rapidly healed. Skin graft 21st day. Well.
26	Carini, A.,[22] 1936	37	M.	No	Perianal reg.	Furuncles anal region 2 yrs., with drainage thick yellow pus. Two large ulcerative lesions 5 cm. length each side anus.	Pos.	Pos.	Neg.	Local antiseptics. Emetine hydrochloride.	Amebae rapidly disappeared following 6 injections emetine. Lesions completely healed.
27	Manson-Bahr,[31] 1937	25	M.	No	Abd. wall	Sigmoidoscopy following rectal hemorrhage showed extensive ulceration. Colostomy. Progressive gangrene abdominal wall.	Pos.	Pos.	Pos.	Emetine. Yatren.	Well. Wound cleared. Necrotic tissue sloughed.
28	Fingerland, A.,[13] 1939	54	M.	Yes	Abd. wall	Dysentery for years. Signs intestinal obstruction on admission. Celiotomy. Annular constriction sigmoid. Colostomy. Onset progressive gangrene abdominal wall to area 20 cm. 2 mo. p.o.	Neg.	Pos.	Pos.		Well. Progressively worse, with spread of gangrene. Died.

(2) Those following drainage of ruptured viscus (appendix, fecal fistula, pericolic abscess, colostomy following resection of large bowel).

(3) Those cases with involvement of perianal skin associated with amebic colitis.

(4) Those cases without any direct connection with viscera (this group is not considered in this report).

The collected cases are tabulated in Table I. Of the authentic cases in the literature, 15 recovered, 11 died and two were not followed. The first group contained the greatest number of cases and the highest mortality rate (Table II). In seven of the 11 cases that died, there was extensive gangrene of the abdominal wall following drainage of a liver abscess. The remaining four deaths were caused by gangrene of abdominal wall following a colostomy for obstruction, drainage of a pericolic abscess, a fecal fistula resulting from a resection of the large bowel for what was thought to be a carcinoma but proved to be a "granuloma," and extensive involvement of the perianal skin associated with a severe amebic colitis.

TABLE II

MORTALITY RATE

Group	No. Cases	Died	Well	Not Followed	Mortality Rate
I.....	12	7	5	0	58.3%
II.....	7	3	4	0	42.8%
III.....	9	1	6	2	11.1%

Of the 15 cases in the literature which recovered, six had involvement of the perianal skin and subcutaneous tissue. Five cases followed drainage of a liver abscess, one followed a colostomy for ulcerative colitis, two cases followed drainage of a ruptured appendix, and one case followed drainage of a perforated diverticulum of the large bowel. The two cases which were not followed had involvement of only the perianal skin.

CASE REPORTS

Case 1.—A. W., colored, female, age 63, a native of Tennessee, entered the Surgical Service of the Vanderbilt University Hospital, November 6, 1933, with the chief complaint of vague abdominal pain of six months' duration. There had been no nausea, vomiting nor diarrhea. Two months before admission she had noticed a mass in the left upper abdominal quadrant, which had subsequently become tender. The mass gradually increased in size. There had been no chills, although she stated positively that she had fever. She had never been out of the state of Tennessee. The remainder of her history was not remarkable.

Physical Examination.—The patient was an extremely ill, poorly nourished, elderly colored woman. Temperature 103° F., pulse 140, respirations 30. The skin was dry and there was evidence of marked loss of weight. Examination of the abdomen revealed a large, firm, tender, fluctuant mass in the left upper abdominal quadrant. The remainder of the examination was not remarkable.

Course in Hospital.—Repeated examinations of the stools were negative for amebae, although the mass was suspected of being an amebic abscess. Her temperature rose daily to 104° F., and she rapidly became worse. On the third hospital day, celiotomy was carried out through a left rectus incision over the mass. A large quantity of foul-smelling, grayish pus was evacuated and a drain was placed in the cavity. Cultures at

this time were positive for the colon bacillus, but cultures for anaerobic organisms were negative. No amebae were found in smears made from the pus. After drainage, the

FIG. 1.—Case 1: Photograph of the lesion. In this case, the ulcerated area is not as extensive as in Case 2, but the gangrenous edge of the ulcer can be plainly seen.

temperature immediately fell, and with transfusions and supportive treatment she rapidly improved.

On the seventh postoperative day, necrosis of the wound was noticed. This rapidly progressed until there was a wide area of gangrene about the draining sinus at the

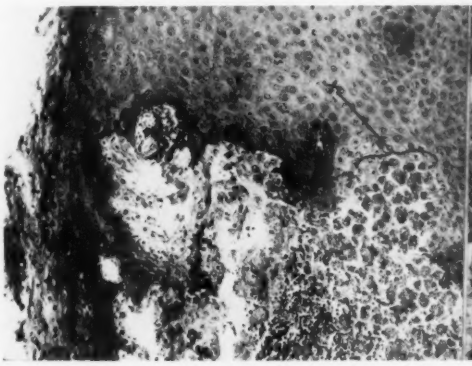

FIG. 2.—Case 1: Photomicrograph of section of skin taken from the periphery of the ulcerated area. The amebae can be seen to be actually invading the epithelium at point indicated by the bracket marked X.

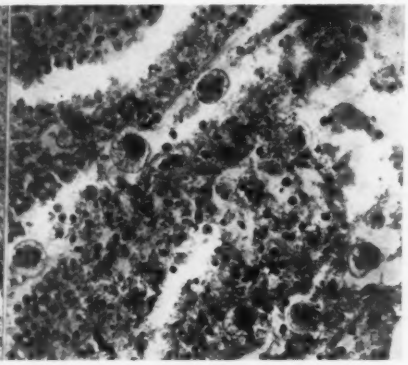

FIG. 3.—Case 1: Photomicrograph showing a section taken from the base of the ulcer. The nuclei in the amebae are prominent. (High magnification.)

bottom of a deep crater, the base of which was bathed in foul-smelling pus (Fig. 1). Around the wide gangrenous area there was an area of erythema. For the first time

motile forms of Endameba histolytica were found. Biopsy of the skin at periphery of ulcerated area revealed the presence of amebae on microscopic section (Figs. 2 and 3). The patient was immediately given emetine hydrochloride 0.03 Gm. twice daily. This was administered over a period of 16 days. The wound was irrigated with Yatren and with Dakin's solution. An extensive débridement was carried out and the wound edges were beveled. Frequent electrocardiographic tracings were made while the emetine was being administered. In spite of this specific treatment, blood transfusions and supportive measures, she lost weight and strength and expired on the fiftieth hospital day. Autopsy was not obtained. Amebae were never found in the stools.

Case 2.—D. E., white, male, age 34, a bricklayer and a native and resident of

FIG. 4.—Case 2: Photograph of the gangrenous area. Here, the massive involvement of the anterior abdominal wall is shown as well as the overhanging edges of the crater.

Tennessee, was admitted to the Surgical Service of Vanderbilt University Hospital August 15, 1939. He was referred because of "sloughing of the abdominal wall." Six months prior to admission he had experienced sudden sharp pain in the right upper abdominal quadrant. The pain remained localized and was unaccompanied by nausea and vomiting. The pain subsided and left him with tenderness in the right upper abdominal quadrant which persisted for about two weeks. Three months later the pain reappeared and became a constant dull ache. Three weeks after reappearance of the pain the patient himself felt a mass in the epigastrium. The mass continued to increase in size and became very tender. There were no concomitant gastro-intestinal symptoms. Two and one-half months later, celiotomy was performed by his local physician, who states that "a right

rectus incision was made over the mass and about 1,500 cc. of thick, pinkish, odorless material was evacuated. The wound was closed with drainage and the patient was discharged two weeks later, still draining profusely."

Three weeks after operation the edges of the wound became gangrenous and this

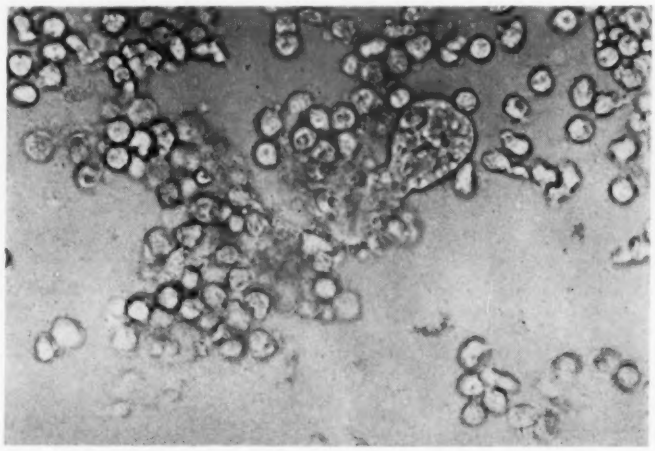

FIG. 5.—Case 2: A motile form of Endameba histolytica recovered from the exudate. The ameba has ingested numerous red blood cells and cellular debris.

process spread rapidly over almost the entire abdominal wall. His condition became rapidly worse, temperature became elevated, he lost weight and strength and became delirious. He was admitted to Vanderbilt University Hospital six weeks after the onset of gangrene of the abdominal wall.

FIG. 6.—Case 2: After extensive débridement. The granulating area has been partially grafted; in spite of that amebae can still be recovered from the draining sinus.

Physical Examination.—The patient was an extremely ill, emaciated, semicomatose, young white male. Temperature 101.2° F., pulse 132, respirations 32. The skin was dry and pale. There was almost complete loss of subcutaneous tissue. Remainder of physical examination was not remarkable except for the abdominal wall. Here, there was an area of ulceration extending from the xiphoid process almost to the symphysis

pubis and laterally to the anterior axillary lines, measuring 22x18 cm. in diameter. The edges of the ulcer were irregular and overhanging. The surrounding skin was black, dry and parchment-like in texture, with an advancing "halo" of deep red, shading gradually into the color of the normal skin. The base of the ulcer was bathed in thick yellowish-

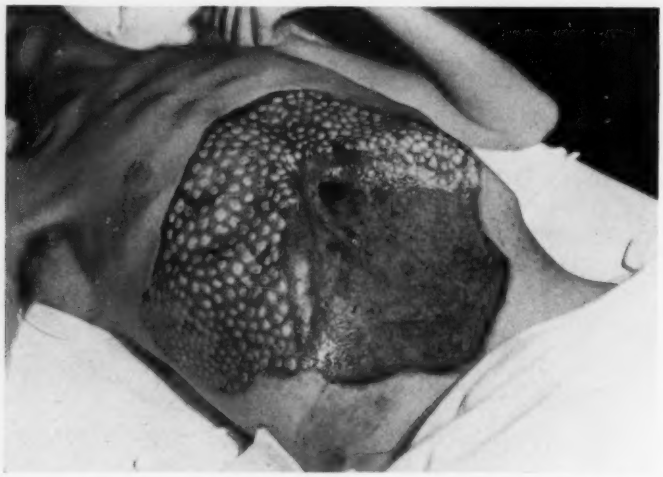

FIG. 7.—Case 2: Showing further grafting. Exudate from the sinus still contains amebae.

green pus which gave off an acrid unpleasant odor. On clearing the crater of purulent material, both rectus abdominalis muscles could be plainly seen, the anterior rectus sheath had been completely digested. In the midline just below the xiphoid and in the superior portion of the crater there was a sinus about 2x3 cm. in diameter which would admit

FIG. 8.—Case 2: Skin grafting almost complete, although amebae are still present. They did not affect the skin transplants.

the index finger for a distance of 4 cm. (Fig. 4). From this sinus exuded yellow bile. The remainder of the physical examination was not remarkable.

Course in Hospital.—Several massive blood transfusions were administered with slight improvement in the general condition. Infestation with Endameba histolytica was

suspected from the very first, but only on the seventh hospital day were the organisms found (Fig. 5). Cultures were positive for an anaerobic streptococcus. Amebae were found at first only under the overhanging edges of the ulcer. As soon as the diagnosis was made, the patient was immediately given emetine hydrochloride (0.065 Gm. intramuscularly daily for 12 days). Amebae were *never* found in the stools. On the tenth hospital day, as soon as his general condition would permit, an extensive débridement of all the necrotic tissue was carried out. This was a rather formidable procedure as it entailed removable of a tremendous amount of tissue. Bleeding was controlled with catgut ligatures and hot wet packs and he was returned to the ward in only fair condition.

The sinus continued to discharge purulent material and smears were positive for amebae. Irrigation of the wound was begun with Dakin's solution and the sinus itself, which continued to discharge bile-stained material, was irrigated with carbazone.

As soon as there was evidence of granulation tissue in the wound, small, deep grafts were applied to the defect at frequent intervals (Figs. 6, 7, 8, 9). It was possible to cover almost the entire area with epithelium although the discharge from the sinus was still positive for Endameba histolytica. The skin transplants were not affected by the organisms.

The patient began to gain weight and strength and was discharged perfectly well after 115 hospital days, with instructions to return at a later date for excision of the grafted area (small, deep grafts) and application of split-grafts.

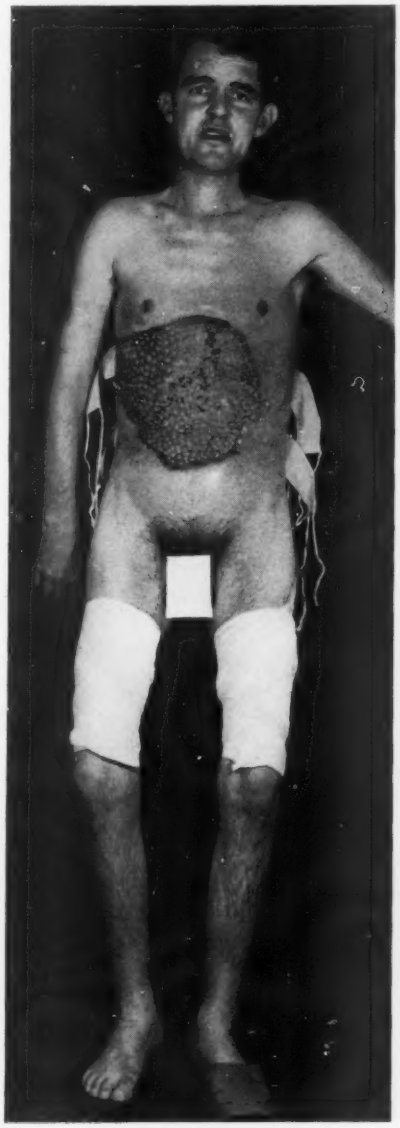

FIG. 9.—Case 2: Skin grafting has been completed and the sinus has completely healed. The state of nutrition of the patient has improved tremendously.

COMMENT.—The most striking action of the Endameba histolytica is lysis of the tissues without a great deal of tissue reaction. The picture is greatly altered, however, when amebae attack the skin around a discharging sinus. The characteristics of this disease are exemplified by Case 2 (Fig. 4) where one sees the rapidly spreading ulcerative process, an irregular crater with overhanging gangrenous edges, "an advancing 'halo' beyond the margin of the ulcer which varies in color from a dusky red through various shades until it merges gradually with the color of the normal skin" (Engman and Meleney[6]). The base of the ulcer is bathed in pus and frequently partially digested anatomic structures may be identified.

Secondary infection of the involved tissue with bacteria plays an important part in the progress of the disease. It is well known that secondary infection of an amebic abscess of the liver greatly increases the gravity of the prognosis. This factor holds true also for amebic ulceration of the skin. In Case 1, the course was complicated by the colon bacillus; in Case 2, an anaerobic streptococcus was present which disappeared soon after irrigations with Dakin's fluid were begun.

From the two foregoing cases and those reported in the literature, it may be seen that involvement of the skin and subcutaneous tissues by Endameba histolytica is an extremely grave complication.

The most important factor in care of amebic ulceration of the skin is *early recognition* of the cause of the disease. In many instances amebiasis has been suspected and repeated examinations of the exudate have been made without finding amebae. It must be borne in mind that smears taken from the discharging sinus will frequently show no amebae while bits of necrotic tissue taken from the undermined, overhanging edges of the crater will yield numerous motile forms.

When the pathologic picture described above is encountered, it is justifiable to administer emetine even if smears are negative for amebae. However, it is important to differentiate this type of skin involvement from progressive postoperative synergistic gangrene caused by micro-aerophilic nonhemolytic streptococcus.

Next in importance to the early administration of emetine is thorough débridement of the involved tissue.

Gangrene of the skin due to amebiasis is almost universally seen in ill-nourished people. Consequently, one must exercise a great deal of thought and patience in their postoperative care. Their diet must be adequate in calories and especially high in protein content, in an effort to combat the hypoproteinemia that they often present. As hospitalization extends over a long period of time, the administration of vitamins is of great value. These patients are usually anemic so that the frequent administration of whole blood is very valuable. Administration of serum or plasma is also helpful in elevating low serum proteins. Skin grafts should be applied to granulating areas as soon as possible.

SUMMARY

Two cases of gangrene and ulceration of the skin of the anterior abdominal wall due to infestation with Endameba histolytica have been presented.

Case 1 was an elderly negress, who developed gangrene of the skin following drainage of a liver abscess. She died on the fiftieth postoperative day in spite of administration of emetine hydrochloride and débridement of the gangrenous tissue. The liver abscess was secondarily infected with the colon bacillus.

Case 2 was a young white male, who also developed very extensive gangrene and ulceration of the abdominal wall subsequent to drainage of a liver

abscess. On the seventh hospital day, motile forms of Endameba histolytica were found and he was given emetine hydrochloride, and extensive débridement of old devitalized tissue was undertaken. The wound granulated and skin grafts were applied. He was discharged perfectly well. In neither of these cases were amebae found in the stools.

A brief résumé of the literature is given. Twenty-eight authentic cases of amebiasis of the skin which were in association with visceral lesions have been collected. Fifteen of these cases recovered, 11 expired, and two were not followed.

Early recognition of the etiology of the disease, early administration of emetine, and extensive débridement of the affected tissue has been emphasized.

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BRIEF COMMUNICATION AND CASE REPORT

FREE TRANSPLANTATION OF FAT FOR BRONCHO-PULMONARY CAVITY*

CASE REPORT

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NEW YORK, N. Y.

Case Report.—J. E., male, age 62, was first admitted to Mount Sinai Hospital, July 18, 1938, with the history of cough and purulent expectoration of seven months' duration. There was also some loss in weight and increasing dyspnea. For two or more weeks before admission, there had been fever and pronounced chest pain. This history of a seven months' illness was preceded by a vague history of having "swallowed a bone." The roentgenogram revealed infiltration in the left lower lobe with a series of pleural fluid levels. By bronchoscopy, much foul pus and fragments of chicken bone were evacuated from the lower lobe.

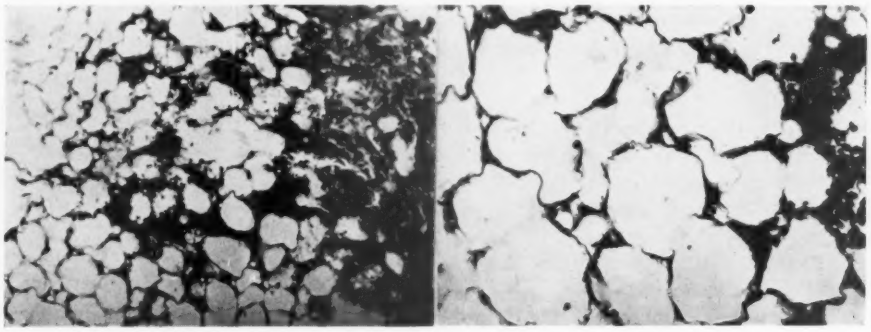

FIG. 1 FIG. 2

FIGS. 1 and 2.—Photomicrographs of a section of the fat graft, removed from the wound 22 days after transplantation. (Low and high powers, respectively.)

Fever continued after the bronchoscopic treatment, but the cough became much reduced and the foul odor became faint. A roentgenogram showed no substantial change. Accordingly, operation was performed for encapsulated pyopneumothorax.

Operation.—Collections of foul pus in the pleura were evacuated through a posterolateral thoracic approach. Multiple perforated pulmonary abscesses comprised the floor of the pyopneumothorax. Several dilated bronchial orifices opened into the wall of the pulmonary cavity. The picture, therefore, was that of a classic "lattice-lung."

The empyema cavity reduced in size progressively after operation. The "lattice-lung" persisted. The patient was discharged with a clean wound and a tube in place leading to the bronchopulmonary cavities.

He was readmitted to the hospital, January, 1939, for closure of the bronchopulmonary cavity. Except for a slight cough he was symptom free. The wound was clean. No infiltration of the lung was invisible in the roentgenogram. By bronchoscopy, there was a

* Presented before the New York Surgical Society, April 26, 1939. Submitted for publication July 7, 1939.

slight amount of secretion in the left main bronchus. The situation thus being satisfactory, transplantation of fat was proceeded with.

Second Operation.—January 3, 1939: The edges of the wound were freshened, the skin mobilized and the roof of the pulmonary cavity split open. The lesion was a typical bronchopulmonary cavity, about one and three-quarter inches in each diameter. There were a number of blowing bronchial fistulae. A mass of fat, of about these proportions, was removed subcutaneously from above the iliac crest and placed into the cavity. It fitted snugly. The graft was held in place by approximating the fibrous tissue which roofed the cavity and the skin by interrupted sutures. On the sixth postoperative day, the sutures were removed, and the wound appeared healed. Two days later, however, a partial separation of the skin was noted. The graft was visible in the depths. There was no bronchial fistula. On the twelfth day after operation, the graft was still seen to be in place, despite the fact that the wound was partly open. No bronchial fistula was present. On the seventeenth day after operation, the graft was seen to be still in place, and was adherent. Granulation tissue partly covered the transplant. There was no bronchial fistula. A specimen of the graft was removed for microscopic examination on the twenty-second day (Figs. 1 and 2). The wound healed not long afterward, and has remained healed. A roentgenogram demonstrated the absence of pulmonary infiltration after operation. The pathologic report of the specimen of the graft which was removed was: "Fat tissue and fibrous tissue connected with granulation tissue. The fat tissue is not necrotic."

DISCUSSION.—DR. CARL EGGERS (New York) said that he had had the pleasure of discussing Doctor Neuhof's original presentation of this subject before the American Thoracic Society two years ago. At that time, Doctor Neuhof had quite a series of cases and reported excellent results, similar to that obtained in the present instance. Doctor Neuhof stated then that the conception of transplantation of fat into a cavity which is partly lined with epithelium, and which is perhaps even moderately infected, did not agree with the ideas he had concerning tissue transplantation, and that it was a rather empiric method. Nevertheless, the facts are irrefutable, in that the majority of cases—17 were reported by Doctor Neuhof at the time—were healed, all except three which were failures, and three which were imperfectly healed. The question came up of what becomes of such a clean fat graft when transplanted into a cavity lined with epithelium; although it may be surgically clean it is not actually sterile. That question is still open, and is rather interesting in view of the present case presentation in which instance Doctor Neuhof reopened the wound, or in which the wound opened itself, and he had occasion to study the graft *in situ* some time after transplantation. He found that—contrary to one's expectation—the graft had actually "taken," and was being vascularized. Doctor Eggers said he doubted such a possibility at the time of the original presentation two years ago. Doctor Neuhof himself felt that probably the graft would not live but would gradually become absorbed, but, while in there, would tend to obliterate the cavity and also favor obliteration of the bronchi. Such a viewpoint was also held by Doctor Churchill at the time. When one realizes the difficulty of closing these cavities by ordinary surgical methods, one learns to appreciate any new procedure that promises results. One probably has to assume that the fat, which molds itself entirely into the cavity, actually does block the bronchi and that vascularization gradually takes place.

Some of these cavities can be obliterated if one brings about favorable conditions for healing; for instance, if one immobilizes the lung sufficiently and excises the thick fibrotic margins and perhaps even approximates the margins of the lung by suture, and then puts a muscular or subcutaneous tissue flap with skin over it. It is well for one who may have a case of this type to operate

upon, to bear both methods in mind. In very rebellious cases resection of the lobe may be indicated.

DOCTOR NEUHOF (closing): As Doctor Eggers implied, the operative procedure of transplantation of fat was empirically conceived. Even at the present time, when I have had a number of successful results, I feel that there is no logical basis for the operation. I thought of it only as an attempt at a short-cut in the first case because nothing else seemed to be feasible in a small child, who was just convalescing from a pneumonotomy and drainage of an unusually large pulmonary abscess.

Concerning the question of actual viability of these fat grafts, all I can say is that I had assumed that they acted only as scaffolds for the ingrowth of connective tissue and underwent gradual and progressive degeneration and absorption. When, however, as in this case, the specimen reveals viability even in the presence of an unsatisfactory set-up for viability, one may have to change one's viewpoint as to degeneration and disappearance of the graft.

Doctor Eggers has assumed that pulmonary cavities after drainage of abscesses become completely lined with epithelium. If this assumption were entirely correct, then a free fat graft or any other tissue graft or tissue flap should not be prone to "take." Although I have no proof, it is my conviction that these cavities are only partly lined with epithelium, and that, here and there, there are areas of granulation tissue. It seems to me that it is from these areas which are not epithelialized that there are sent forth vascular sprouts which represent the first stage of the maintenance of nourishment of the graft.

FORUM

(Articles published in the ANNALS OF SURGERY *do not necessarily represent the opinions of the editors, even though they are selected and published with editorial approval. Likewise, the editors may not necessarily be in agreement with correspondents whose communications are important if only because they present stimulating opposition. Since this impartial point of view is vital to progress in science, the* ANNALS OF SURGERY *offers this forum for pertinent discussions of reasonable length.*—ED.)

Re: **New Incision for Closed Space Infection (Felon) Involving Distal Phalanx of Finger:—by Jerome J. Weiner, M.D. (Annals of Surgery, 111, 126-134, Jan., 1940)**

FREDERICK CHRISTOPHER, M.D., EVANSTON, ILL.:

"First, I would strongly advise against amputation of the tuft of the distal phalanx, no matter whether it seems to be involved in infection or not. If osteomyelitis has developed it would seem far better to me to wait for sequestration. Regeneration of the phalanx will usually occur. Second, I think it very important not to damage the periosteum of the distal phalanx in any surgical procedure. The incision should be limited to the soft parts. Third, I believe that removal of the nail is unnecessary and painful and that it prolongs disability. Fourth, I believe that making the incision in the highly vascularized area of the nail bed is unwise and unnecessary. Once the correct diagnosis of felon has been made, it seems to me that the chief therapeutic indication is the relief of tension, which, if unrelieved, may invite necrosis of some of the distal phalanx. The relief of tension is also important to permit drainage of the abscess and to relieve pain. For this purpose, in my opinion, the hockey-stick incision is by far the best, and should not be of such depth as to nick the periosteum. The high incidence of felon and the prolonged morbidity even with proper treatment make this really an important question."

SUMNER L. KOCH, M.D., CHICAGO:

"Doctor Weiner's suggestions as to the treatment of felon seem to me to violate the first law of surgery, 'Do no harm,' on every count. To avulse the nail is not a simple injury; it requires from five to seven weeks, sometimes longer, for the formation of a new nail. Why one should voluntarily add this not trivial and totally unnecessary injury to the finger with an infection in the anterior closed space is difficult to comprehend. Furthermore, an incision through the nail bed, as depicted in Plate I, No. 3, would almost invariably lead to a fissured and deformed nail. Bone involvement often occurs following infection of the anterior closed space, but the patient will recover most rapidly and certainly if the soft tissues are drained adequately and the bone is left alone. To amputate the tip of the phalanx and expose haversian canals and bone cells to infection may lead to the very involvement that is most likely to result in long-delayed healing and loss of bone substance. That such a complication actually did take place following operation in the third case, reported by Doctor Weiner, is suggested by a comparison of Figures 10 and 11. While in some cases the abscess may be close to the tip of the finger, in many others, it lies at some distance from it. To cut the normal and uninfected tissue to reach an abscess which could be drained by an incision directly over it does not seem wise or commendable. Finally to entrust the care of an infected wound to the patient and instruct him 'to soak the finger in hot boric solution every two hours for 20 minutes' is a fairly certain way of adding further infection to the open wound."

HUBLEY R. OWEN, M.D., PHILADELPHIA:

" . . . I do think that Doctor Weiner's article . . . on the subject of The Treatment of Felons is terrible, and exactly contrary to all of the teaching of Kanavel, which we have tried to follow. The idea of locally infiltrating 1% novocain into a thumb which was 'tense, tender and hot' shows a very limited knowledge of surgery, and I do not believe this article should have been published in the ANNALS."

REBUTTAL TO THE OBJECTIONS OF DOCTORS CHRISTOPHER, KOCH AND OWEN

JEROME J. WEINER, M.D.

NEW YORK, N. Y.

THE QUESTIONS raised by Doctors Christopher, Koch and Owen are:

First, that avulsing of the nail is a traumatizing procedure, and it takes from five to seven weeks for a new nail to regenerate; that where the nail regenerates it is fissured and deformed. The illustrations in my original communication of Cases 1 and 3 show the nail in Case 1 to be primarily fissured (Fig. 5). In Case 3, however, it regenerated quite normally. The bone has also regenerated. Assuming the nail is fissured in some instances, is it not preferable to give a patient a fissured nail rather than a deformed, mutilated and desensitized finger? Most of my cases show an initial fissured nail which ultimately is replaced by a normal one.

Second, they contend that bone involvement often occurs following infection of the anterior closed space, but the patient will recover most rapidly, and certainly, if the soft tissues are drained adequately and the bone is left alone. That to amputate the tip of the phalanx exposes the haversian canals and bone cells to further involvement. Two cases operated upon, subsequent to the original article, had the tuft of the bone removed; the indication for its removal being necrosis of Sharpey's fibers which were closely attached to the periosteum. In both these cases, the healing period was shortened by at least four weeks. Two other cases also showed necrosis of Sharpey's fibers. However, the tip of the phalanx was not removed. Both these cases required a longer period of time to heal as compared with the two preceding ones.

Third, Doctor Koch feels that, in some cases, the abscess may be close to the tip of the finger. If the abscess is close to the tip of the finger, beware of a collar-button abscess. Case 3, of my original article, was just such a type of case—and the patient pricked that superficial abscess herself. The subsequent roentgenograms revealed what happened. I wish to state to Doctor Koch that I did not remove the tuft of the bone in this case. I treated it along the lines suggested by both him and Doctor Christopher, namely, incising the soft tissues without removing the bone. After a period of time, the necrotic connective tissue sloughed away and, later, the diseased bone sequestrated itself and the wound commenced healing. I feel that had I removed the tuft of bone in this case, together with the necrotic connective tissue, I would probably have arrested the process and thus shortened the healing period. No doubt, Doctors Koch and Christopher have seen many incisions made in the median line for what appeared to be a superficial abscess of the tip of the finger. How many of these cases developed osteomyelitis due to inadequate drainage? No instance of anterior space infection can be adequately drained unless Sharpey's fibers are completely divided. Neither the median nor the lateral hockey-stick incisions accomplish this. Invariably, a thick plug of necrotic connective tissue blocks drainage and the infection is forced into the bone cells and haversian canals. Necrosis of the bone ensues and only when the sequestrum is extruded, does healing take place. The "fish-mouth" incision, while it provides adequate drainage, gives results as may readily be demonstrated. An eighth patient demonstrated what occurs in cases where inadequate drainage is obtained, and probes are used to ascertain the presence of sequestra. Incisions in this case were made through the nail.

Fourth, Doctor Kanavel, in his book on hand infections, claims that there is nothing superior to the ordinary dressing, saturated with hot boric acid solution, to wall-off an acute process.

Doctor Owen received an erroneous impression when he read my article. The local infiltration of 1 per cent novocain was by the simple method of block anesthesia, a procedure which is generally endorsed. The site of injection is at least two inches from the infection. It was perhaps an oversight not to have mentioned this obvious step in technic in my original communication.

I agree with Doctor Owen that a general anesthetic is the anesthesia of choice; however, did it occur to Doctor Owen that the economic factor had to be reckoned with in a majority of my cases? To spend but one day in the hospital costs the patient a minimum of $35 and up ($15 for operating room, $10 for anesthesia, $5 for board, $5 for laboratory fee). I have employed local anesthesia in most of my cases.

I firmly believe that the incision I have employed has a great deal of merit, because all of the major objections are overcome and the end-results are good.

JEROME J. WEINER, M.D.,
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MEMOIR

DOCTOR GATEWOOD

1887–1939

BY THE UNTIMELY DEATH of Doctor Gatewood, of Chicago, on May 22, 1939, the Middle West has lost one of the most prominent of its younger surgeons.

DOCTOR GATEWOOD

Doctor Gatewood was the eldest son of Annie L. Pierrot and Dr. Wesley Emmet Gatewood, and was born October 11, 1887, in the little town of Stockport, Ohio, where his father, a graduate of the Medical Schools of Dartmouth and Bellevue, had come to practice. His elementary school education was received in Nashville, Tennessee, the place to which the family had moved

because of his father's failing health, and he graduated from the High School in Nashville in 1903, entering the Ohio State University in the fall of that year. He received the degree of A.B. from that institution in 1907, and that of M.A. in 1910, his research problems for the Master's degree having been undertaken in the departments of physiology and anatomy.

He began his medical work at the Ohio State University during the years 1907–1910, and was graduated from Rush Medical College in Chicago in 1911. Following this, a year was spent in the Pathology Laboratory at Michael Reese Hospital, and he served his internship at the Presbyterian Hospital under Dr. A. D. Bevan, where he continued as resident and associate in Doctor Bevan's service for several years.

Like all members of the surgical staff of the Presbyterian Hospital, Doctor Gatewood came up through the ranks as a teacher in surgery in Rush Medical College. Starting as an assistant in 1914, he held a Fellowship in 1918, was an instructor of surgery in 1919, an assistant clinical professor in 1923, an associate professor in 1929, and clinical professor of surgery in 1937, which position he held until the time of his death. Doctor Gatewood was always a student of surgery and throughout his surgical career was engaged in some type of experimental work.

His literary contributions cover a wide field, but he was particularly interested in that part of abdominal surgery having to do with the stomach and duodenum. As a teacher, he probably had no superior on the Rush Faculty, and it is a question whether anyone else in that group enjoyed an equal amount of respect and admiration on the part of the Rush medical students.

Recognition of Doctor Gatewood's caliber as a surgeon came early and continued through the years. Besides his membership in the American Medical Association, and the state and local medical societies, he enjoyed the distinction of belonging to the Chicago Surgical Society, the Western Surgical Association, the American College of Surgeons, and the American Surgical Association. He was among the Founders' Group of the American Board of Surgery.

Doctor Gatewood is survived by his wife, Esther Harper, to whom he was married in 1923, his son Emmet, and his daughters Helen and Mary Jean. His residence at the time of his death was in Highland Park, Illinois, where, among his civic interests was a membership on the School Board, in which work he took a very active part.

We, his colleagues, who have grown up with him since our intern days and have worked with him at Presbyterian Hospital, at Rush Medical College, and at the Cook County Hospital recognized him to be not only a most capable surgeon and a great teacher but a man of the highest quality. His sincerity of purpose, honesty, and modesty won for him not only the admiration of all those with whom he came in daily contact but the love of those who knew him best. In his sudden passing, at the age of 52, we feel an irreparable loss.

EDWIN M. MILLER, M.D.

Great Britain Needs Surgical Equipment, Medical Supplies, Drugs, Sera, Hospital Beds, etc. . . . To Meet the Greatest Crisis in Her History!

THE Medical and Surgical Supply Committee, composed of 250 physicians and surgeons in principal cities throughout the United States, is urgently in need of instruments, dressings, biologicals, pharmaceuticals and equipment to be shipped to Great Britain for distribution among hospitals and medical field stations.

Complete operation units for General and Traumatic Surgery, as well as special units for Ear, Nose and Throat; Plastic; Brain; Orthopedic; and Genito-Urinary Surgery are desperately required.

Doctors are urged to send these materials immediately to the Medical and Surgical Supply Committee of America, 420 Lexington Ave., New York City.

Advisory Chairmen: Dr. Carnes Weeks, Dr. Franz Groedel, Dr. Allen O. Whipple, Dr. Stuart L. Craig, Dr. Conrad Berens, Dr. Joseph Felsen, Dr. Malcolm Goodridge.

CONDENSED REPORT

The Medical and Surgical Supply Committee was formed and is functioning under a Department of State permit, No. 357, dated August 7, 1940.

An appeal was made to the doctors of New York City, to join in a nation-wide campaign for surgical and medical supplies, with which to equip emergency stations and field hospitals, to relieve the present crisis in England. To date 164 cases, estimated value $47,000, have been shipped to Great Britain.

The Committee is composed almost exclusively of physicians and surgeons, and the work is carried on under their supervision and advice. The success of the Committee's efforts has been due to a large extent to the wonderful support the physicians and surgeons have received from other doctors, hospitals and pharmaceutical wholesalers and retailers.

Rigid standards of inspection have been set up by the Committee; all supplies and equipment received are inspected by experts before being packed for shipment. The existing abnormal conditions under which the unpacking will be made causes this effort on our part to be much appreciated.

EDITORIAL ADDRESS

Original typed manuscripts and illustrations submitted to this Journal should be forwarded prepaid, at the author's risk, to the Chairman of the Editorial Board of the ANNALS OF SURGERY

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Contributions in a foreign language when accepted will be translated and published in English.

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